UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**

For the fiscal year ended December 31, 2021.

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**

For the transition period from to .

Commission file number: 001-35347

Clovis Oncology, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**90-0475355**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
5500 Flatiron Parkway, Suite 100 Boulder, Colorado	**80301**
(Address of principal executive offices)	**(Zip Code)**

(303) 625-5000

(Registrant's telephone number, including area code)

Not Applicable

(Former name, former address and former fiscal year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act

Title of Each Class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock par Value $0.001 per share	CLVS	The NASDAQ Global Select Market

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405) of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company, and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock, par value $0.001 per share, held by non-affiliates of the registrant on June 30, 2021, the last business day of the registrant's most recently completed second quarter, was $671,298,229 based on the closing price of the registrant's common stock on the NASDAQ Global Select Market on that date of $5.80 per share.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of February 22, 2022 was 142,244,650.

DOCUMENTS INCORPORATED BY REFERENCE Portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2022 Annual Meeting of Stockholders, which is to be filed within 120 days after the end of the registrant's fiscal year ended December 31, 2021, are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated therein.

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PART I

This Annual Report filed on Form 10-K and the information incorporated herein by reference includes statements that are, or may be deemed, "forward-looking statements." In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this Annual Report on Form 10-K and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, the market acceptance and commercial viability of our approved product, the development and performance of our sales and marketing capabilities, the performance of our clinical trial partners, third party manufacturers and our diagnostic partners, our ongoing and planned non-clinical studies and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, including our ability to confirm clinical benefit and safety of our approved product through confirmatory trials and other post-marketing requirements, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, expectations regarding sales of our products, our results of operations, financial condition, liquidity, our ability to raise capital, prospects, growth and strategies, the industry in which we operate, including our competition and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity and the development of the industry in which we operate may differ materially from the forward-looking statements contained herein.

Any forward-looking statements that we make in this Annual Report on Form 10-K speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this Annual Report on Form 10-K or to reflect the occurrence of unanticipated events.

You should also read carefully the factors described in the "Risk Factors" section of this Annual Report on Form 10-K to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. You are advised, however, to consult any further disclosures we make on related subjects in our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and our website.

Clovis Oncology®, the Clovis logo and Rubraca® are trademarks of Clovis Oncology, Inc. in the United States and in other selected countries. All other brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to "Clovis," the "Company," "we," "us" and "our" refer to Clovis Oncology, Inc., together with its consolidated subsidiaries.

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company focused on acquiring, developing and commercializing innovative anti-cancer agents in the United States, Europe and additional international markets. We target our development programs for the treatment of specific subsets of cancer populations, and simultaneously develop, with partners, for those indications that require them, diagnostic tools intended to direct a compound in development to the population that is most likely to benefit from its use.

Rubraca® is an oral small molecule inhibitor of poly ADP-ribose polymerase ("PARP") marketed in the United States for two indications specific to recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and also an indication specific to metastatic castration-resistant prostate cancer ("mCRPC"). The initial indication received approval from the United States Food and Drug Administration ("FDA") in December 2016 and covers the treatment of adult patients with deleterious *BRCA* (human genes associated with the repair of damaged DNA) mutation (germline and/or

somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. Rubraca received a second approval from FDA in April 2018 for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Diagnostic testing is not required for patients to be prescribed Rubraca in this maintenance treatment indication.

In May 2020, the FDA also approved Rubraca for the treatment of adult patients with mCRPC associated with a deleterious *BRCA* mutation (germline and/or somatic) who have been treated previously with androgen receptor-directed therapy and a taxane-based chemotherapy and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. The FDA approved this indication under accelerated approval based on objective response rate and duration of response data from the TRITON2 clinical trial. As an accelerated approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The TRITON3 clinical trial is expected to serve as the confirmatory study for Rubraca's approval in mCRPC as well as the basis for us to seek a potential second-line label expansion. We anticipate the initial data readout from TRITON3 in the second quarter of 2022.

In Europe, the European Commission granted a conditional marketing authorization in May 2018 for Rubraca as monotherapy treatment of adult patients with platinum-sensitive, relapsed or progressive, *BRCA* mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum-based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy. In January 2019, the European Commission granted a variation to the marketing authorization to include the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. With this approval, Rubraca is authorized in Europe for certain patients in the recurrent ovarian cancer maintenance setting regardless of their *BRCA* mutation status. Following successful reimbursement negotiations, Rubraca is marketed in each of Germany, United Kingdom, Italy, France, Spain, the Netherlands and Switzerland.

Beyond our labeled indications, we have a clinical development program underway to further evaluate Rubraca in a variety of solid tumor types, either as monotherapy or in combination with other agents, including the ATHENA Phase 3 study as part of our ongoing clinical collaboration with Bristol Myers Squibb Company ("Bristol Myers Squibb") to evaluate its immunotherapy OPDIVO® (nivolumab) in combination with Rubraca. We anticipate initial data from two independent readouts for ATHENA during 2022: Rubraca monotherapy versus placebo (ATHENA-MONO) in the second quarter of 2022, with results of the separate analysis of Rubraca in combination with Opdivo (ATHENA-COMBO) anticipated in the fourth quarter of 2022.

The three anticipated data readouts, ATHENA-MONO, ATHENA-COMBO and TRITON3 discussed above, provide the potential to obtain approvals that reach larger patient populations in earlier lines of therapy for ovarian and prostate cancers. Following availability of top-line results from ATHENA-MONO, we plan to file a supplemental New Drug Application ("sNDA") with the FDA and request a variation to the European MAA, and we plan to do the same for the subsequent TRITON3 and ATHENA-COMBO anticipated data readouts, assuming, in each case, that the Phase 3 clinical data is supportive.

The timing for each Phase 3 data readout is contingent upon the occurrence of the protocol-specified progression free survival ("PFS") events, and timing estimates are based on event-based projections.

We hold worldwide rights to Rubraca.

FAP-2286 is our initial product candidate to emerge from our targeted radionuclide therapy collaboration with 3B Pharmaceuticals GmbH ("3BP"). FAP-2286 is a peptide-targeted radionuclide therapy ("PTRT") and imaging agent targeting fibroblast activation protein ("FAP"). PTRT uses cancer cell-targeting peptides to deliver radiation-emitting radionuclides specifically to tumors. Following the clearance by FDA of two INDs submitted in December 2020 to support the use of FAP-2286 as an imaging and treatment agent, we initiated the phase 1 portion of the LuMIERE clinical study in June 2021. LuMIERE is a phase 1/2 study of FAP-2286 labeled with lutetium-177 (^{177}Lu-FAP-2286) evaluating the compound in patients with advanced solid tumors to determine the dose, schedule, and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development

program. FAP-2286 labeled with gallium-68 (^{68}Ga-FAP-2286) is being utilized to identify tumors that contain FAP for treatment in this study.

During 2022, we also anticipate the first presentation of phase 1 data from LuMIERE at nuclear medicine-focused meetings, additional presentations of non-clinical data for FAP-2286 and the launch of our combination study program to explore FAP-2286 in combination with other oncology compounds, and in 2023, a potential IND filing of FAP-2286 linked to a FAP-targeted alpha-emitter PTRT.

We hold U.S. and global rights to FAP-2286, excluding Europe (defined to include Russia, Turkey and Israel), where 3BP retains rights.

We are also collaborating with 3BP on a discovery program directed to up to three additional, undisclosed targets for targeted radionuclide therapy, to which we would have global rights for any resulting product candidates.

Lucitanib, our product candidate currently in clinical development, is an investigational, oral, potent angiogenesis inhibitor which inhibits vascular endothelial growth factor receptors 1 through 3 ("VEGFR1-3"), platelet-derived growth factor receptors alpha and beta ("PDGFR α/β") and fibroblast growth factor receptors 1 through 3 ("FGFR1-3"). Lucitanib inhibits the same three pathways as Lenvima® (lenvatinib), which has received an FDA approval for use in certain populations of patients with endometrial cancer in combination with Keytruda® (pembrolizumab), a PD-1 inhibitor. This, together with preclinical data for lucitanib in combination with a PD-1 inhibitor that demonstrated enhanced anti-tumor activity compared to that of single agents, represent a scientific rationale for development of lucitanib in combination with a PD-1 inhibitor, and in February 2019, lucitanib was added to our clinical collaboration with Bristol Myers Squibb. The phase 1b/2 LIO-1 study is evaluating the combination of lucitanib and Opdivo in gynecologic cancers. Interim data from the non-clear cell ovarian cancer expansion cohort were presented at ASCO 2021 and the initial efficacy data do not support further development in non-clear cell ovarian cancer. The remaining three cohorts, which include non-clear cell endometrial, cervical and clear-cell ovarian and endometrial cancers, showed sufficient responses in stage one of each of the cohorts to advance to stage 2. The data from the cervical cohort have been accepted as a plenary presentation at the Society of Gynecologic Oncology (SGO) 2022 Annual Meeting on Women's Cancer in March 2022 and represent encouraging data in this subset of gynecological cancers. However, given the competing priorities, including development of FAP-2286, we have determined that we will not pursue further development of lucitanib in gynecological cancers at this time.

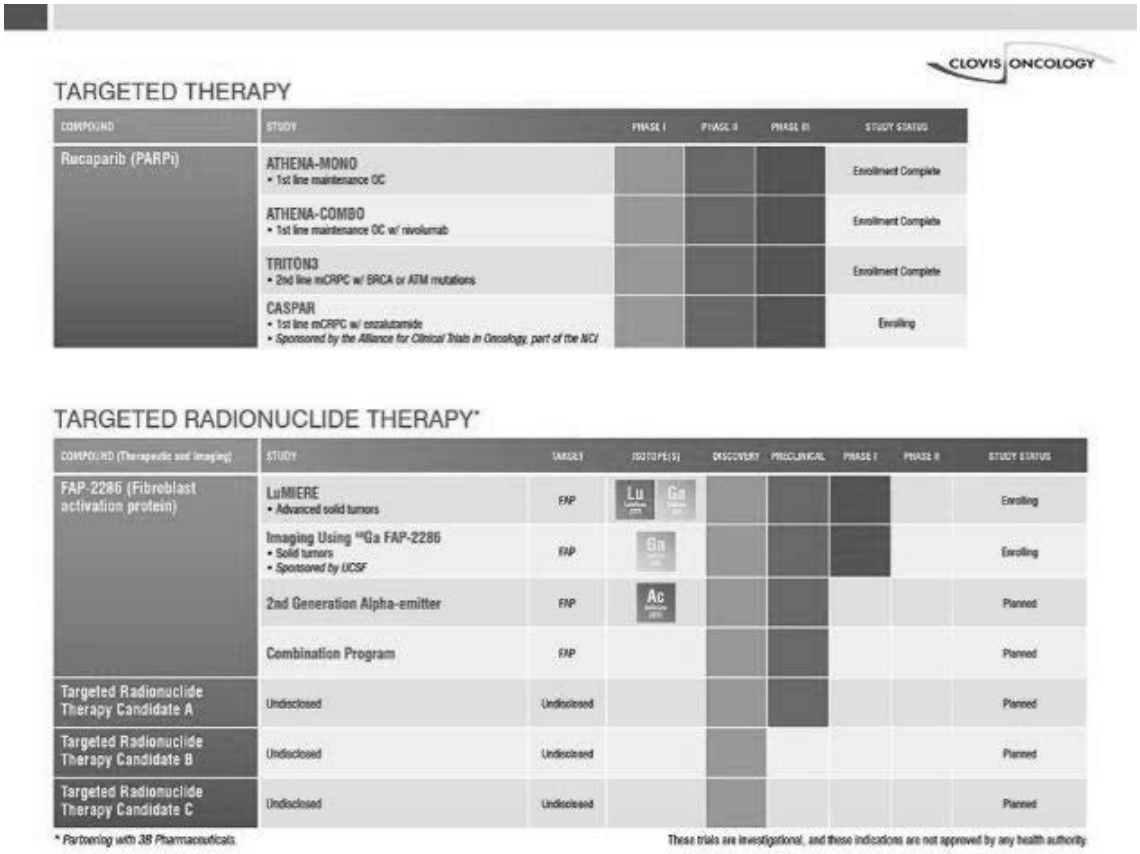
We hold the global (excluding China) development and commercialization rights for lucitanib.

Clovis was founded in 2009. We have built our organization to support innovative oncology drug development for the treatment of specific subsets of cancer populations. To implement our strategy, we have assembled an experienced team with core competencies in global clinical and non-clinical development, regulatory operations and commercialization in oncology, as well as establishing collaborative relationships with companies specializing in companion diagnostic development.

We have three key strategies on which we remain focused: first, we seek to drive Rubraca revenue growth; second, we intend to grow our targeted radionuclide therapy program, which includes the currently enrolling LuMIERE phase 1/2 clinical study of FAP-2286, which is the PTRT targeting FAP; and third, we seek to achieve long-term financial stability.

Our Products and Development Strategy

We continue to evaluate the use of Rubraca for selected patient populations and, where appropriate, collaborate with partners for companion diagnostic development. We have focused our development strategy for Rubraca on indications where we believe patient populations exhibit higher frequencies of mutant *BRCA* tumors or tumors with other homologous recombination deficiencies ("HRD"), where PARP inhibitors have demonstrated clinical or pre-clinical activity in tumors. In the emerging field of targeted radionuclide therapy, our lead candidate, FAP-2286 targets fibroblast activation protein, which is highly expressed across multiple solid tumor types, and is a target of increasing interest for oncology drug development. The following table summarizes the principal ongoing or planned Clovis- or collaborator-sponsored studies:



In certain of these trials, we or our collaborators may have access to interim data on a periodic or continuing basis that will not be made available publicly on the same timeframe as such data becomes available to us, or at all.

Rubraca – a PARP Inhibitor

Overview

Rubraca is an oral, small molecule inhibitor of PARP1, PARP2 and PARP3. We in-licensed Rubraca from Pfizer, Inc. in June 2011 and hold exclusive worldwide rights. Rubraca has received regulatory approvals in the United States and Europe for patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer. Rubraca also received regulatory approval in the United States as a monotherapy treatment of adult patients with *BRCA1/2*-mutant recurrent, metastatic castrate-resistant prostate cancer.

In the United States, Rubraca is approved by the FDA for the treatment of adult patients with deleterious *BRCA* (human genes associated with the repair of damaged DNA) mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. *BRCA* mutations are believed to occur in approximately 25% of women with ovarian cancer. In April 2018, based on positive date from the phase 3 ARIEL3 clinical trial described below, the FDA granted a second approval for Rubraca for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy, a broader and earlier-line indication. Diagnostic testing is not required for patients to be prescribed Rubraca in this maintenance treatment indication.

Rubraca is also approved in the United States for the treatment of adult patients with mCRPC associated with a deleterious *BRCA* mutation (germline and/or somatic) who have been treated previously with androgen receptor-directed therapy and a taxane-based chemotherapy and selected for therapy based on an FDA-approved companion diagnostic for

Rubraca. The FDA approved this indication in May 2020 under accelerated approval based on objective response rate and duration of response data from the TRITON2 clinical trial. As an accelerated approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The TRITON3 clinical trial, anticipated to read out in the second quarter of 2022, is expected to serve as the confirmatory study for Rubraca's approval in mCRPC as well as a potential second-line label expansion.

In Europe, Rubraca is authorized for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy regardless of their *BRCA* mutation status. Following successful reimbursement negotiations, Rubraca has been launched in each of Germany, United Kingdom, Italy, France, Spain, the Netherlands and Switzerland.

The Role of PARP Inhibition in Cancer Therapy

Cells in the human body are under constant attack from agents that can cause damage to DNA, including sunlight and other forms of radiation, as well as DNA-binding chemicals that can cause changes in the composition of DNA. Cells have evolved multiple mechanisms to enable such DNA repair, and these mechanisms are complementary to each other, each driving repair of specific types of DNA damage. If a cell's DNA damage repair system is overwhelmed, then the cell will die undergoing a form of suicide termed apoptosis. A fundamental principle of cancer therapy is to damage cells profoundly with radiation or DNA-binding drugs, such as alkylating agents or platinums, to induce apoptosis, and thus cancer cell death. Multiple DNA repair mechanisms active in the cell may reduce the activity of these anti-cancer therapies.

The PARP family comprises 17 structurally related proteins that have been identified on the basis of sequence similarity. PARP1, PARP2, and PARP3 play a central role in DNA repair. They are rapidly recruited to the sites of DNA damage and catalyze the recruitment of additional proteins that initiate the repair of damaged DNA. The breast cancer 1 ("*BRCA1*") and breast cancer 2 ("*BRCA2*") genes also have important roles in DNA repair pathways such as homologous recombination. According to the National Cancer Institute, *BRCA1* and *BRCA2* mutations are associated with an increased risk of ovarian, breast, prostate, and pancreatic cancers.

Rubraca is an inhibitor of PARP enzymes, including PARP1, PARP2, and PARP3. PARP inhibitors have shown activity in *BRCA1/2* mutant and homologous recombination ("HR") repair deficient cancer cell lines through a mechanism known as synthetic lethality in which the loss of two genes/pathways is required for cell death. The inhibition/inactivation of repair pathways by administration of a PARP inhibitor in the context of an underlying genetic defect such as a *BRCA* mutation results in tumor cell death through accumulation of unrepaired DNA damage.

Alterations in DNA repair genes other than *BRCA1/2* have been observed in, and contribute to the hereditary risk of, ovarian, breast, prostate and pancreatic cancers. PARP inhibitors have shown evidence of nonclinical and clinical activity in tumors with alterations in non-*BRCA* HR genes. DNA repair deficiencies resulting from genetic and epigenetic alterations can result in a "*BRCA*-like" phenotype that may also render tumor cells sensitive to PARP inhibitors. One approach to identify patients with DNA repair deficiencies due to mechanisms other than a mutation in *BRCA* or other non-*BRCA* HR genes is to assess loss of heterozygosity ("LOH"), or the loss of one normal copy of a gene, which arises from error-prone DNA repair pathways when HR is compromised.

On the basis of these scientific observations, we initially developed Rubraca in ovarian cancer patients with tumors having *BRCA* mutations or other HRD, and these molecular markers will be further explored in the Rubraca Phase 3 studies anticipated to read out during 2022.

Ovarian cancer

According to the American Cancer Society, an estimated more than 19,000 women will be diagnosed with ovarian cancer in the United States and there will be an estimated nearly 13,000 deaths from ovarian cancer in 2022, and according to GLOBOCAN in 2020, an estimated 66,000 women in Europe are diagnosed each year with ovarian cancer, and ovarian cancer is among those cancers with the highest rate of deaths. According to the NIH National Cancer Institute, more than 75% of women are diagnosed with ovarian cancer at an advanced stage.

Rubraca's approvals in the U.S. and Europe in the recurrent *BRCA* mutant ovarian cancer treatment setting were based on data from two multicenter, single-arm, open-label clinical trials, Study 10 (NCT01482715) and ARIEL2 (NCT01891344), in women with advanced *BRCA*-mutant ovarian cancer who had progressed after two or more prior chemotherapies. All patients received Rubraca orally 600 mg twice daily as monotherapy. Treatment continued until disease progression or unacceptable toxicity. The primary efficacy outcome measure of both studies was objective response rate (ORR) as assessed by the investigator according to Response Evaluation Criteria in Solid Tumors ("RECIST") version 1.1. Results from a blinded independent radiology review ("BICR") were consistent.

The efficacy of Rubraca in the ovarian cancer maintenance treatment setting was investigated in ARIEL3 (NCT01968213), a double-blind, multicenter clinical trial in which 564 patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who were in response to platinum-based chemotherapy were randomized (2:1) to receive Rubraca tablets 600 mg orally twice daily (n=375) or placebo (n=189). Treatment was continued until disease progression or unacceptable toxicity. All patients had achieved a response (complete or partial) to their most recent platinum-based chemotherapy. Randomization was stratified by best response to last platinum (complete or partial), time to progression following the penultimate platinum therapy (6 to < 12 months and ≥ 12 months), and tumor biomarker status. The major efficacy outcome was investigator-assessed PFS evaluated according to RECISTv1.1.

The primary efficacy analysis evaluated three prospectively defined molecular sub-groups in a step-down manner: 1) tumor *BRCA* mutant ("tBRCAmut") patients, inclusive of germline and somatic *BRCA* mutations (n=196); 2) HRD patients, including tBRCAmut patients and *BRCA* wild-type with high LOH (n=354), and, finally, 3) the intent-to-treat population, or all patients treated in ARIEL3 (n=564). ARIEL3 demonstrated a statistically significant improvement in PFS for patients randomized to Rubraca as compared with placebo in all patients, and in the HRD and tBRCAmut subgroups. Median PFS in the tBRCAmut patients was 16.6 months (95% CI: 13.4–22.9) in the Rubraca group (n=130) versus 5.4 months (95% CI: 3.4–6.7) in the placebo group (n=66) (Hazard Ratio, or HR: 0.23 [95% CI: 0.16–0.34]; p<0.0001). Median PFS in the HRD patients was 13.6 months (95% CI: 10.9–16.2) in the Rubraca group (n=236) versus 5.4 months (95% CI: 5.1–5.6) in the placebo group (n=118) (HR: 0.32 [95% CI: 0.24–0.42]; p<0·0001). Median PFS in the intent-to-treat population was 10.8 months (95% CI: 8.3–11.4) in the Rubraca group (n=375) versus 5.4 months (95% CI: 5.3–5.5) in the placebo group (n=189) (HR: 0.36 [95% CI: 0.30–0.45]; p<0·0001). An exploratory analysis in the HRD/*BRCA* wild-type population demonstrated a median PFS of 9.7 months (95% CI: 7.9–13.1) in the Rubraca group (n=106) versus 5.4 months (95% CI: 4.1–5.7) in the placebo group (n=52) (HR: 0.44 [95% CI: 0.29–0.66]); p<0.0001).

BICR results were consistent. In a pre-specified analysis of the key stand-alone secondary endpoint of progression-free survival assessed by BICR, PFS was also improved in the Rubraca group compared with placebo in all three populations. Median PFS in the tBRCAmut patients was 26.8 months (95% CI: 19.2 to not reached) in the Rubraca group versus 5.4 months (95% CI: 4.9–8.1) in the placebo group (HR: 0.20 [95% CI: 0.13–0.32]; p<0.0001). Median PFS in the HRD patients was 22.9 months (95% CI: 16.2 to not reported) in the Rubraca group versus 5.5 months (95% CI: 5.1–7.4) in the placebo group (HR: 0.34 [95% CI: 0.24–0.47]; p<0.0001). Median PFS in the intent-to-treat population was 13.7 months (95% CI: 11.0–19.1) versus 5.4 months (95% CI: 5.1–5.5) in the placebo group (HR: 0.35 [0.28–0.45]; p<0.0001). An exploratory analysis in the HRD/*BRCA* wild-type population demonstrated a median PFS of 11.1 months (95% CI: 8.2-NR) in the Rubraca group (n=106) versus 5.6 months (95% CI: 2.9–8.2) in the placebo group (n=52) (HR: 0.55 [95% CI: 0.35–0.89]; p=0.0135).

Enrollment in ARIEL3 included one-third of patients who had achieved a complete response to their prior platinum-based therapy, and two-thirds of patients who had achieved a partial response to their prior platinum-based therapy. Of those with a partial response, 37% had measurable disease at the time of enrollment and were therefore evaluable for response. The confirmed overall response rate by investigator-assessed RECISTv1.1 in the tBRCAmut group treated with Rubraca was 37.5% (15/40), of these, 17.5% (7/40) were complete responses. This compared with 9% (2/23) in the placebo group (p=0.0055). No complete responses were seen in the tBRCAmut placebo group. RECIST responses were also observed in *BRCA* wild-type HRD-positive and *BRCA* wild-type HRD-negative subgroups. In a subsequent post hoc exploratory analysis of ARIEL3 data, a higher response rate was also seen in patients without measurable disease in both the tBRCAmut group and the intent to treat population (inclusive of BRCAmut patients) as compared to placebo. RECIST responses were not assessed by independent blinded review.

Safety data from ARIEL3 demonstrated consistency with prior Rubraca studies. Treatment emergent adverse events ("TEAEs") in the ARIEL3 Rubraca group were generally managed with dose modifications and not associated with increased mortality or morbidity compared with the placebo group. The most common (occurring in ≥5% of patients)

TEAEs of grade ≥3 reported in patients treated with Rubraca in the ARIEL3 study were anemia/decreased hemoglobin (21%), increase in ALT/AST (10%), neutropenia (7%), asthenia/fatigue (7%) and thrombocytopenia (5%). The discontinuation rate for TEAEs (excluding disease progression) was 15% for Rubraca-treated patients and 2% for the placebo arm. In ARIEL3, the rate of treatment-emergent myelodysplastic syndrome ("MDS")/acute myeloid leukemia ("AML") in the Rubraca arm was <1% (3/372), and no patients on the placebo arm experienced treatment-emergent MDS/AML. In approximately 1,100 patients treated with Rubraca, MDS/AML occurred in 10 patients (0.9%), including those in long term follow-up. Of these, 5 occurred during treatment or during the 28-day safety follow-up (0.5%). The duration of Rubraca treatment prior to the diagnosis of MDS/AML ranged from 1 month to approximately 28 months. The cases were typical of secondary MDS/cancer therapy-related AML; in all cases, patients had received previous platinum containing chemotherapy regimens and/or other DNA damaging agents.

At the time of the analysis of PFS, overall survival (OS) data were not mature (with 22% of events). The comprehensive dataset for ARIEL3 was presented at the 2017 European Society of Medical Oncology ("ESMO") Congress in early September 2017 and subsequently published in *The Lancet*. The ARIEL3 dataset formed the basis for sNDA filed with the FDA as well as the marketing authorization variation filed with the EMA supporting the approval of Rubraca in the US in April 2018 and Europe in January 2019 respectively, as maintenance treatment in adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

The ARIEL4 confirmatory study (NCT 02855944) is a Phase 3 multicenter, randomized study of Rubraca versus chemotherapy, which enrolled 349 relapsed ovarian cancer patients with *BRCA* mutations (inclusive of germline and/or somatic) who had received two or more prior lines of chemotherapy. The primary endpoint of the study is investigator-assessed progression-free survival ("InvPFS"), with a step-down analysis from the efficacy population (if significant) to the intent to treat ("ITT") population. The efficacy population comprised the group of patients with a deleterious tumor BRCA mutation and excluded those with a BRCA reversion mutation as determined by a blood test. Development of reversion mutations that restore BRCA protein function are associated with resistance to platinum-based chemotherapies and PARP inhibitors in BRCA-mutant cancers, and these occur more frequently in platinum-resistant vs platinum-sensitive patients (13% and 2% respectively in the ARIEL2 study).

In December 2020, we announced that Rubraca met the primary study endpoint of significantly improving InvPFS versus chemotherapy in the primary efficacy population with a hazard ratio of 0.64 (p=0.001). The median PFS for the patients in the efficacy population treated with rucaparib was 7.4 months versus 5.7 months among those who received chemotherapy. Additionally, in the ITT population, the rucaparib arm achieved statistical significance over the chemotherapy arm for the primary endpoint of PFS with a hazard ratio of 0.67 (p=0.002). The median PFS for the patients in the ITT population treated with rucaparib was 7.4 months versus 5.7 months among those who received chemotherapy. Adverse events were consistent with the known safety profiles of Rubraca and chemotherapy. Patients with a BRCA reversion mutation represented 7% of patients enrolled in the study and as anticipated, InvPFS results for those patients showed limited benefit from Rubraca therapy. An interim analysis of overall survival, a secondary endpoint in the study in which 51% of events had occurred in the intent-to-treat population, showed a trend toward an overall survival advantage in the chemotherapy arm, but was confounded by the high rate (64%) of per-protocol crossover to Rubraca following progression on chemotherapy. An analysis of the ITT population of patients showed a trend toward an OS advantage for those patients who received Rubraca at any point in the trial versus those who did not. ARIEL4 study results were presented at the Society of Gynecologic Oncology Virtual Annual Meeting on Women's Cancer (SGO) in March 2021. Completion of ARIEL4 is a post-marketing commitment in the U.S. and Europe and the clinical study report for the trial has been submitted to the regulatory authorities for review to satisfy this commitment.

Prostate cancer

The American Cancer Society estimates that approximately 268,000 men in the United States will be diagnosed with prostate cancer in 2022, and the GLOBOCAN Cancer Fact Sheets estimated that approximately 473,000 men in Europe were diagnosed with prostate cancer in 2020. Castrate-resistant prostate cancer has a high likelihood of developing metastases. Metastatic castrate-resistant prostate cancer ("mCRPC") is an incurable disease, usually associated with poor prognosis. Approximately 43,000 men in the U.S. are expected to be diagnosed with mCRPC in 2020. According to the American Cancer Society, the five-year survival rate for mCRPC is approximately 30%. A number of publications have reported germline or somatic mutations in *BRCA1* or *BRCA2* are approximately 12% in mCRPC according to an article published in JCO Precision Oncology in 2017. These molecular markers may be used to select patients for treatment with a PARP inhibitor.

The TRITON (Trial of Rucaparib in Prostate Indications) program in prostate cancer initiated in the second half of 2016, and currently includes two Clovis-sponsored studies. Enrollment is complete for both TRITON2 and TRITON3.

The TRITON2 study (NCT02952534) is a multicenter Phase 2 single-arm study of Rubraca in men with mCRPC that enrolled patients with *BRCA* mutations (inclusive of germline and/or somatic) or other deleterious mutations in other homologous recombination repair genes. Patients in the TRITON2 study have received prior treatment with at least one androgen receptor ("AR")-directed therapy and one previous line of taxane-based chemotherapy and were screened for a deleterious germline or somatic mutation in *BRCA1*, *BRCA2* or one of 13 other pre-specified homologous recombination ("HR") genes. Study participants were allocated into three cohorts based on the type of gene mutation and disease status, as determined by genomic sequencing and RECIST criteria, respectively. Each cohort receives 600 mg Rubraca twice daily and are grouped based on the following criteria: A) mutation in either *BRCA1*, *BRCA2* or ATM genes, with tumors that can be measured with visceral and/or nodal disease; B) mutation in either *BRCA1*, *BRCA2* or ATM genes, with tumors that cannot be measured with visceral and/or nodal disease, or C) mutation in another HR gene associated with sensitivity to PARP inhibition, with or without measurable disease. The primary study endpoints include confirmed ORR and duration of response ("DOR") per modified RECIST v.1.1/PCWG3 criteria assessed by BICR in patients with measurable disease at baseline by independent review and PSA response in patients with no measurable disease at baseline. Secondary endpoints include overall survival ("OS"), clinical benefit rate, and safety and tolerability.

Efficacy and safety data from TRITON2 formed the basis of a sNDA that was submitted to FDA in late 2019. Evaluable patient populations in the sNDA dataset included the following: 62 RECIST-evaluable patients with a *BRCA* (germline and/or somatic) mutation and measurable disease (BICR); 115 patients with a *BRCA* (germline and/or somatic) mutation and measurable or non-measurable disease; and 209 patients with HRD-positive mCRPC. The RECIST-evaluable patient population demonstrated a 44% ORR (N=62; 95% CI 31, 57) by BICR. Objective response rates were similar for patients with a germline *BRCA* versus somatic *BRCA* mutation. Median DOR was not evaluable at data cut-off. Additionally, a 55% confirmed PSA response rate (95% CI 45, 64) was observed in an analysis of 115 patients with a deleterious *BRCA* mutation (germline and/or somatic) and measurable or non-measurable disease.

TRITON2 evaluated the safety of Rubraca 600 mg twice daily as monotherapy treatment in the 209 patients with HRD-positive mCRPC enrolled in the study, including the 115 with *BRCA*-mutated mCRPC. The most common adverse reactions (greater than or equal to 20% of patients; CTCAE Grade 1-4) occurring in the *BRCA* mutant population (n=115) were asthenia/fatigue, nausea, anemia, ALT/AST increased, decreased appetite, constipation, rash, thrombocytopenia, vomiting, and diarrhea. The most common laboratory abnormalities (greater than or equal to 35% of patients; CTCAE Grade 1-4) were increase in ALT, decrease in leukocytes, decrease in phosphate, decrease in absolute neutrophil count, decrease in hemoglobin, increase in alkaline phosphatase, increase in creatinine, increase in triglycerides, decrease in lymphocytes, decrease in platelets, and decrease in sodium.

In May 2020, the FDA approved Rubraca for the treatment of adult patients with mCRPC associated with a deleterious BRCA mutation (germline and/or somatic) who have been treated previously with androgen receptor-directed therapy and a taxane-based chemotherapy and are selected for therapy with an FDA-approved companion diagnostic. The FDA approved this indication under accelerated approval based on objective response rate and duration of response data from the TRITON2 clinical trial. As an accelerated approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The TRITON3 clinical trial is expected to serve as the confirmatory study for Rubraca's approval in mCRPC. Foundation Medicine's blood based diagnostic test, FoundationOne Liquid CDx, approved by the FDA in August 2020, is a companion diagnostic for the detection of deleterious BRCA mutation (germline and/or somatic) to select mCRPC patients for treatment with Rubraca.

The TRITON3 study (NCT02975934) is a Phase 3 comparative study in men with mCRPC enrolling *BRCA* mutant and ATM (both inclusive of germline and/or somatic) patients who have progressed on AR-targeted therapy and who have not yet received chemotherapy in the castrate-resistant setting. TRITON3 will compare Rubraca to physician's choice of AR-targeted therapy or chemotherapy in these patients. The planned primary endpoint of the study is radiologic PFS. TRITON3 initiated during the first quarter of 2017, and topline data from TRITON3 are anticipated in the second quarter of 2022, contingent upon the occurrence of the protocol-specified number of PFS events.

The Alliance for Clinical Trials in Oncology is sponsoring the Phase 3 CASPAR study (NCT04455750) comparing the combination of enzalutamide and Rubraca to enzalutamide alone in mCRPC. The study, which is currently enrolling

patients, is expected to enroll approximately 1,000 patients in the United States at National Clinical Trials Network ("NCTN") sites nationally and is currently the only study evaluating the combination of a PARP inhibitor and a novel anti-androgen with an overall survival endpoint. The Alliance is part of the NCTN sponsored by the National Cancer Institute. CASPAR is currently enrolling patients.

LODESTAR tumor-agnostic study

The LODESTAR clinical study (NCT04171700) is a Phase 2 study evaluating Rubraca as monotherapy treatment in patients with recurrent solid tumors associated with a deleterious mutation in a homologous recombination repair ("HRR") gene across a variety of tumor types. The primary cohort includes patients with tumor mutations in *BRCA1*, *BRCA2*, *PALB2, RAD51C, RAD51D* as well as an exploratory cohort that includes patients with tumor mutations in several additional genes. The study initiated in late 2019 and based on initial results from the ongoing study, we saw encouraging evidence of activity in patients with a biallelic tumor mutation of *BRCA* or other target genes. Importantly, for *BRCA*-mutated breast and pancreatic and certain other tumors types, the majority of tumors have biallelic loss. Despite these encouraging data in a molecularly-defined subset of patients, we have determined that the expected time to enrollment and the requirement to conduct a confirmatory study in this population do not represent a sufficiently significant opportunity to pursue further, as compared to our other alternatives, including development of FAP-2286.

Opdivo combination trials

Our ongoing collaboration with Bristol Myers Squibb involves the evaluation of the combination of Rubraca with Bristol Myers Squibb's immunotherapy Opdivo® (nivolumab) in ovarian cancer in the Phase 3 ATHENA study.

We believe that a preclinical rationale supports the potential of the combination of our PARP inhibitor Rubraca with immune checkpoint inhibitors such as the PD-1 inhibitor Opdivo. *BRCA1* and *BRCA2* and other HRD mutations are associated with increased tumor mutational burden, which may create additional tumor-specific antigens or "neoepitopes." Increased tumor mutation burden has been shown to correlate with increased benefit from immune checkpoint blockade. In addition, cell death that is induced by a PARP inhibitor is considered immunogenic and stimulates a "STING-like" pathway due to fragmented DNA release into cytosol. In mice studies, rucaparib and an anti-PD-1 antibody demonstrated anti-tumor activity in *BRCA1* mutant ovarian tumors. The combination of rucaparib and either an anti-PD-L1 or anti-CTLA-4 antibody were equally compelling in preclinical studies.

The Clovis-sponsored Phase 3 ATHENA study is evaluating the combination of Rubraca and Opdivo, and in February 2019, lucitanib was added to the clinical collaboration in combinations with Opdivo.

ATHENA is a four-arm first-line maintenance treatment study (NCT03522246) to evaluate Rubraca and Opdivo, Rubraca, Opdivo, and placebo in approximately 1,000 newly diagnosed patients with stage III/IV high-grade ovarian, fallopian tube, or primary peritoneal cancer who have completed platinum-based chemotherapy. The primary objectives are first, to determine if Rubraca extends PFS versus placebo (ATHENA-MONO), and second, to determine if the combination of Rubraca and Opdivo meaningfully extends PFS versus Rubraca monotherapy (ATHENA-COMBO). The ATHENA study, which initiated in 2018 and completed enrollment in the second quarter of 2020, evaluates Rubraca in terms of two key outcomes in a step-down manner: monotherapy versus placebo in the first-line maintenance setting in the HRD population, inclusive of *BRCA*, and in the all comers (intent-to-treat) population, and later, any potential advantage for the combination of Rubraca and Opdivo in the all comers (intent-to-treat) population. ATHENA is the first front-line switch maintenance study to evaluate a PARP inhibitor as monotherapy and in combination with an anti-PD-1 in one study design. We anticipate the results of the Rubraca monotherapy arm versus placebo in all study populations in the second quarter of 2022, and then, during the fourth quarter of 2022, the results of Rubraca plus Opdivo versus Rubraca in the intent-to-treat study population. The timing of the two ATHENA readouts (ATHENA-MONO and ATHENA-COMBO) contingent upon the occurrence of the protocol-specified PFS events.

The phase 1b/2 LIO-1 study is evaluating the combination of lucitanib and Opdivo in gynecologic cancers. Interim data from the non-clear cell ovarian cancer expansion cohort was presented at ASCO 2021 and the initial efficacy data does not support further development in non-clear cell ovarian cancer. The remaining three cohorts, which include non-clear cell endometrial, cervical and clear-cell ovarian and endometrial cancers, showed sufficient responses in stage one of each of the cohorts to advance to stage 2. The data from the cervical cohort have been accepted as a plenary presentation at the Society of Gynecologic Oncology (SGO) 2022 Annual Meeting on Women's Cancer in March 2022 and represent encouraging data in this subset of gynecological cancers. However, given the competing priorities,

including development of FAP-2286, we have determined that we will not pursue further development of lucitanib in gynecological cancers at this time.

Bristol Myers Squibb sponsored the CheckMate 9KD (NCT03338790), a Phase 2 three-arm study in mCRPC, evaluating Opdivo + Rubraca, Opdivo + docetaxel + prednisone, and Opdivo + enzalutamide, with the objective of determining how the combinations affects objective response rate and PSA response. The study, which initiated in the fourth quarter of 2017, completed enrollment of patients with biomarker negative or positive disease, for whom tumor tissue samples were used to determine biomarker status. Bristol Myers Squibb presented data from this study at medical meetings during 2021, which showed that the combination showed clinical efficacy in a population of patients with mCRPC who are HR-deficient either pre- or post-chemotherapy, with noteworthy activity in patients harboring *BRCA* mutations. Clinical activity was limited in patients with HR proficient tumors. The safety profile of the combination was as expected based on the individual components, with no new safety signals, and longer follow up and potentially a comparative study is needed to better characterize the clinical benefits of adding Opdivo to rucaparib in this patient population. Ongoing biomarker analyses will further explore potential predictors of treatment benefit of the combination among patients in the post-chemotherapy population.

Bristol Myers Squibb sponsored FRACTION-GC (NCT02935634), a Phase 2 multi-arm study evaluating Opdivo in combination with other therapies in advanced gastric cancer. The trial includes, among other combinations, an evaluation of Opdivo + Rubraca, Yervoy + Rubraca and the triplet combination of Opdivo + Yervoy + Rubraca. While a safe and tolerable safety profile was observed for these Rubraca-containing combinations, efficacy was not demonstrated in this immunotherapy-naïve, heavily pre-treated patient population, and accordingly, the study of these combinations in this population of patients with gastroesophageal cancer is to be completed in 2022.

Companion Diagnostics

Three FDA-approved companion diagnostic tests are commercially available to select cancer patients for treatment with Rubraca.

Foundation Medicine, Inc. ("Foundation") markets its comprehensive companion diagnostic test for solid tumors, FoundationOne®CDx ("F1CDx"), a next generation sequencing-based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations, and copy number alterations in 324 genes (including *BRCA1/2*), select gene rearrangements, as well as genomic signatures, including LOH, microsatellite instability and tumor mutational burden using tumor tissue specimens. F1CDx is approved as a companion diagnostic to select ovarian cancer patients with *BRCA1/2* mutations for treatment with Rubraca.

In August 2020, Foundation received approval for FoundationOne Liquid CDx, a qualitative next generation sequencing-based in vitro diagnostic test that analyzes mutations in 311 genes (including *BRCA*1/2) utilizing circulating cell-free DNA isolated from plasma derived from peripheral whole blood. FoundationOne Liquid CDx is approved as a companion diagnostic to select mCRPC and ovarian cancer patients with *BRCA*1/2 mutations for treatment with Rubraca.

BRACAnalysis CDx®, is a blood-based assay for the qualitative detection and classification of germline mutations in *BRCA1/2* genes commercialized by Myriad Genetics Laboratories, Inc. BRACAnalysis CDx is approved as a companion diagnostic to select ovarian cancer patients with *BRCA1/2* mutations for treatment with Rubraca.

FAP-2286 and Radionuclide Therapy Development Program

FAP-2286 is an investigational diagnostic and therapeutic agent targeting fibroblast activation protein ("FAP"). In September 2019, we acquired U.S. and global rights to FAP-2286, excluding Europe (inclusive of Russia, Turkey and Israel), where 3B Pharmaceuticals, the discoverer of FAP-2286, retains rights. In addition to our collaboration on FAP-2286 development, we are also collaborating with 3BP on a discovery program directed to up to three additional, undisclosed targets for targeted radionuclide therapy, to which we would obtain global rights for any resulting product candidates.

Patent applications are pending that claim FAP-2286 generically and specifically (including with respect to composition of matter) that, if issued, would have expiration dates in 2040.

The Role of Fibroblast Activation Protein as a Radiopharmaceutical Target

FAP is highly expressed in cancer-associated fibroblasts ("CAFs") which are found in the majority of cancer types, potentially making it a suitable target across a wide array of solid tumors. CAFs are highly prevalent in the tumor microenvironment of many cancers and persist through all malignant stages of a tumor, from primary tumor to metastasis. FAP has limited expression on normal fibroblasts, reducing the potential for effects in normal tissue.

PTRT is an emerging class of drugs in oncology and involves the systemic administration of a small amount of radioactive emitting material – a radionuclide – that is conjugated to a peptide for use as a targeted pharmaceutical. The peptide is able to recognize and bind to specific targets on the cancer cells or in their microenvironment, and the intended result is to deliver a high dose of radiation to the tumor while sparing normal tissue because of its rapid systemic clearance. Radionuclides with different emission properties, primarily beta particles or more potent alpha particles, are used to deliver cytotoxic radiation to the tumor-associated targets. In order for the targeted radiopharmaceutical to be safe and efficacious, it must rapidly attach to cancer cells or in close vicinity to the cancer cells, be retained in or at the tumor site for a sufficient period of time that the radionuclide can have activity on the cancer cells, have minimal attachment to non-cancer cells, and then be rapidly cleared from the body. In most cases, the radionuclides may be visualized by using nuclear medicine imaging techniques to evaluate the specificity of the agent, supporting a precision medicine approach to delivery of the therapeutic form of the agent.

Clinical studies of small molecule imaging agents targeting FAP have validated this target in a diverse number of cancer indications and support the further evaluation of PTRT. FAP-targeted radiopharmaceuticals have at least two potential modes of anti-tumor activity: radiation crossfire, in which tumor cells are irradiated due to their close proximity to CAFs; and depletion of CAFs, disrupting the communication between the tumor cells and the tumor stroma. In addition, in certain tumor types, such as sarcoma and mesothelioma, FAP is expressed on the tumor cells themselves, and in those tumors, FAP-targeted radiopharmaceuticals may have a direct antitumor effect.

In addition, an evident biological rationale supports the combination of targeted radionuclide therapy with cancer therapies including PARP inhibitors and anti-PD(L)-1 agents. While our initial development focus will be on monotherapy with FAP-2286, we intend to explore these types of combinations pre-clinically and clinically as well.

The FAP-2286 product candidate consists of a peptide that selectively binds to FAP and a linker and site to which radioactive medical isotopes can be attached for use as an imaging agent or therapeutic agent. Our initial development plans include the use of gallium-68 (^{68}Ga) as an imaging agent and lutetium-177 (^{177}Lu) as a therapeutic agent.

The anti-tumor efficacy of ^{177}Lu-FAP-2286 has been evaluated preclinically in FAP-expressing tumor models. Data presented at the 2020 ESMO Virtual Congress demonstrated that a single, IV dose of ^{177}Lu-FAP-2286 resulted in statistically significant tumor growth inhibition in two different mouse xenograft models: (1) HEK293 cells stably transfected with human FAP (HEK-FAP); and (2) Sarc4809 sarcoma patient-derived xenograft model with endogenous FAP expression.

Nonclinical data evaluating FAP expression across a variety of solid tumor types were presented at the AACR-NCI-EORTC conference in October 2021. High FAP expression was observed in multiple indications, including pancreatic ductal adenocarcinoma, cancer of unknown primary, salivary gland, mesothelioma, colon, bladder, sarcoma, squamous NSCLC, as well as squamous head and neck cancers. In these tumor types, high FAP expression was detected in both primary and metastatic tumor samples and was independent of tumor stage or grade. The analysis also demonstrated that in most tumor types, FAP expression was predominantly localized to cancer-associated fibroblasts ("CAFs") surrounding the tumor cells and integrated into the tumor microenvironment. In addition, in cancers of mesenchymal origin including sarcoma and mesothelioma, expression was observed in tumor cells in addition to CAFs. These data support the investigation of FAP-2286 in multiple tumor types in the planned phase 2 expansion cohorts of LuMIERE. Additional presentations of nonclinical and initial presentations of clinical data are anticipated at nuclear medicine meetings during 2022.

First Clinical Experience Reported from FAP-2286 Named Patient Use

Physicians in Germany and certain other countries may treat patients suffering from life-threatening diseases or disease leading to severe disability with experimental drugs if no other appropriate options are available under named-patient or similar programs. A physician may initiate treatment for specific patients until there is commercial product

available and patients are encouraged to enroll in clinical trials where possible. Named patient programs are not clinical trials and the treating physician is solely responsible for, and makes all decisions independently, including dose and assessment of efficacy and safety, and the drug sponsor has no role in decisions.

In December 2019, Professor Dr. Richard P. Baum reported his initial independent clinical experience with FAP-2286 in named-patient use in eleven patients at the International Centers for Precision Oncology Foundation Symposium in Bad Berka, Germany. At Prof. Dr. Baum's clinic, FAP-2286 was linked to ^{68}Ga as a tumor-imaging compound using PET/CT scanning and to lutetium-177 as a therapeutic agent. The data were published in the Journal of Nuclear Medicine during 2021.

As the early named patient use in Germany suggests, significant interest already exists within the academic community to explore the potential of FAP as an imaging and treatment target.

Our FAP-2286 Clinical Development Plan

We submitted two INDs for FAP-2286 for use as imaging and treatment agents in December 2020 to support an initial phase 1/2 study to determine the dose, schedule and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development program. The FDA cleared the two INDs and we initiated the phase 1 LuMIERE clinical study in June 2021. LuMIERE is a phase 1/2 study of lutetium-177 (^{177}Lu) labelled FAP-2286 (^{177}Lu-FAP-2286) and is evaluating the compound in patients with advanced solid tumors. FAP-2286 gallium-68 (^{68}Ga) labelled FAP-2286 (^{68}Ga-FAP-2286) will be utilized to identify patients with FAP-positive tumors appropriate for treatment in this study.

The ongoing phase 1 portion of the LuMIERE study, for which enrollment in the second dose cohort is currently ongoing, is evaluating the safety of ^{177}Lu-FAP-2286 and will identify the recommended Phase 2 dose and schedule of the investigational therapeutic agent in patients with FAP-positive tumors determined by ^{68}Ga-FAP-2286. Once the phase 2 dose is determined, phase 2 expansion cohorts are planned in multiple tumor types and are expected to initiate in the second half of 2022.

Identification of the tumor types for exploration in phase 2 development is a considerable focus of ours, as the high levels of FAP expression observed in multiple tumor types makes selecting a limited number of tumor types in such expansion cohorts challenging. We believe we will have the opportunity to evaluate a minimum of seven tumor types in a single protocol pan-tumor study with predetermined stopping and accelerating enrollment criteria in each of these tumor types. We believe FAP-2286 provides us with the potential to seek accelerated approvals in multiple tumor types.

During 2022, we also anticipate the first presentations of phase 1 data from the ongoing LuMIERE study at nuclear medicine-focused meetings, as well as the launch of our combination study program to explore FAP-2286 in combination with other oncology compounds. In addition, we anticipate a potential IND filing of FAP-2286 linked the alpha-emitting radionuclide, actinium-225 (^{225}Ac) as a distinct PTRT therapeutic during 2023.

In addition to our ongoing and planned studies, the University of California San Francisco is sponsoring two separate, investigator-initiated, imaging-only studies with ^{68}Ga labeled FAP-2286. The first study, NCT04621435 investigates the utility of ^{68}Ga-FAP-2286 to detect metastatic cancer in solid tumors. The second study, NCT05180162, evaluates the ability of ^{68}Ga-FAP-2286 to identify pathologic fibrosis in the setting of hepatic, cardiac and pulmonary fibrosis. Both studies are currently enrolling.

Preclinical Evaluations

While we are focused clinically on FAP-2286 monotherapy development in our ongoing LuMIERE study, pre-clinically we are evaluating a number of FAP-2286 drug combinations. *Cancer Discovery* and *Journal of Immunology* have reported nonclinical studies demonstrating that FAP-expressing CAFs exert a potent immunosuppressive activity that can promote tumor progression and, according to *Molecular Cancer*, can confer resistance to immune-based therapies such as PD-1/PD-L1 blockade. We are currently evaluating the efficacy and mechanism-of-action of FAP-2286 and a PD-1 monoclonal antibody in syngeneic mouse tumor models.

In addition, a number of publications, including *Scientific Reports, Molecular Cancer Therapeutics* and *Frontiers in Pharmacology*, report non-clinical support for the combination of targeted radiotherapy with PARP inhibitors to

augment efficacy. Radiotherapies work by causing DNA damage via radioactive emission, and if this damage is not repaired, the cell will eventually die. These nonclinical studies also report that inhibition of PARP may augment efficacy in combination with multiple TRT agents. Based on this, we are currently preclinically evaluating the combination of FAP-2286 with our PARP inhibitor, Rubraca, in tumor models.

Lastly, *Scientific Reports, Clinical Oncology* and the *European Journal of Nuclear Medicine and Molecular Imaging* have published data showing that radiation is known to synergize with a number of agents that are currently approved as the standard-of-care in specific cancer indications. For example, *Nuclear Medicine and Biology* reports that gemcitabine, used as a first line chemotherapy in pancreatic cancer and other carcinomas, is a well-known radiosensitizer and could have utility in combination with FAP-2286. We are currently performing a high throughput screen of approved oncology drugs in combination with radiation to identify additional potential combinations for FAP-2286 development.

Lucitanib – a VEGFR, PDGFR and FGFR Inhibitor

Lucitanib is an investigational, oral, potent angiogenesis inhibitor which inhibits vascular endothelial growth factor receptors 1 through 3 ("VEGFR1-3"), platelet-derived growth factor receptors alpha and beta ("PDGFR α/β") and fibroblast growth factor receptors 1 through 3 ("FGFR1-3").

The composition of matter patent for lucitanib expires in 2030 in the U.S. and 2028 in Europe, with up to five years patent term extension available. We hold the global (excluding China) development and commercialization rights for lucitanib.

VEGF, PDGF and FGF: The Role of these Tyrosine Kinase Inhibitors in Cancer

The VEGFs are a family of related extracellular proteins that normally regulate blood and lymphatic vessel development in humans. They act by binding to and activating VEGF receptors, which are cell surface proteins that transmit growth signals to specific cells that are involved in the development of new blood vessels. Certain VEGFs promote growth of multiple solid tumors by stimulating the formation of new blood vessels to feed the tumor and allow it to grow and metastasize. Tumors produce an excessive amount of VEGF. This results in excess VEGFR signaling and the formation of new blood vessels within the tumor. The VEGF ligands that induce angiogenesis are often present in a wide range of cancer indications, including a type of kidney cancer called renal cell carcinoma, a type of liver cancer called hepatocellular carcinoma, gastric cancer, head and neck cancers and other solid tumors.

The PDGF family consists of five different isoforms of PDGF ligand that bind to and activate cellular responses through two different receptors (PDGFRα/ß). In tumors, PDGF signaling plays a diverse role in many aspects of tumor development promoting cell proliferation, invasion, migration and angiogenesis. Amplification and/or mutation of the gene encoding the PDGFRα receptor is observed in a wide range of cancers, including lung cancer, an aggressive form of brain cancer called glioblastoma and a cancer of the gastrointestinal tract known as gastrointestinal stromal tumors. Amplification of the PDGFRα gene results in excess production, or the over-expression, of PDGFRα protein on the surface of the tumor cell. The over-expression of PDGFRα on the tumor cell surface leads to an increased receptor signaling, which stimulates uncontrolled proliferation of some types of tumor cells.

The FGFs are a family of related extracellular proteins that normally regulate cell proliferation and survival in humans. The FGF family consists of 22 ligands that exert their physiological effect on cells by binding to four FGFRs (FGFR1- 4). As with the PDGF family, some cancers display FGF/FGFR gene amplification/mutation resulting in continual activation of the FGFR signaling pathway leading to uncontrolled cell division. Tumors with a relatively high incidence of FGF aberrations, which include amplification of the FGFR1 gene and amplification of a region of chromosome 11q that contains several FGF ligands, include breast and lung cancers. In addition, FGFR gene amplification/mutation is also observed in a wide range of cancer indications including sarcoma, ovarian cancer, adenocarcinoma of the lung, bladder cancer, colorectal cancer and endometrial cancer.

As an inhibitor of VEGFR1-3, PDGFRα/ß and FGFR1-3 and given the role that each of these receptor kinases plays in tumor progression and metastasis formation, lucitanib has the potential benefit of targeting three relevant pro-angiogenic growth factors in targeted patient populations identified by molecular markers. Data from earlier studies suggest that lucitanib's VEGF inhibition may be the primary driver of its activity, and both preclinical and clinical data provide a scientific rationale for further development on lucitanib in combination with other agents.

Targeting angiogenesis and immune checkpoint pathways may have a synergistic effect on antitumor activity. Angiogenesis has been shown to be immunosuppressive within the tumor microenvironment, dampening anti-tumor immune responses, according to Nature Reviews in Clinical Oncology (Fukumura 2018). Immune effects of angiogenesis include modulation of T-cell infiltration into the tumor, inhibition of dendritic cell maturation, and the modulation of cell adhesion molecules and immune cell populations. Inhibition of angiogenesis by small molecule RTK inhibitors or monoclonal antibodies may reverse immunosuppression. These data suggest the clinical activity of PD-(L)1 inhibitors may be enhanced through the inhibition of angiogenesis by lucitanib. Clovis preclinical studies of multiple syngeneic tumor models have shown that lucitanib in combination with a PD-1 inhibitor delivers superior activity. Multiple Phase 1-3 studies are examining the combination of angiogenesis and PD-(L)1 inhibitors in different indications.

Lucitanib inhibits the same three pathways as Lenvima (lenvatinib), which has shown encouraging results when combined with the PD-1 inhibitor Keytruda (pembrolizumab), and this combination has been approved by the FDA on an accelerated basis for the treatment of certain forms of endometrial cancer. This, together with preclinical data for lucitanib in combination with a PD(L)-1 inhibitor as described above, represent a scientific rationale for development of lucitanib in combination with a PD(L)-1 inhibitor, and in February 2019, lucitanib was added to our clinical collaboration with Bristol Myers Squibb evaluating combinations with Opdivo.

LIO-1 is an open-label, Phase 1b/2 study (NCT04042116) of lucitanib in combination with Opdivo in advanced gynecologic cancers and other solid tumors to determine the recommended dose of lucitanib in combination with Opdivo in patients with an advanced solid tumor (Phase 1b); followed by evaluation of the safety and efficacy of lucitanib and Opdivo in patients with an advanced gynecological solid tumor (Phase 2), including ovarian, endometrial and cervical cancers. The primary efficacy endpoint of the LIO-1 study is ORR as assessed by the investigator according to RECIST v1.1.

Interim data from the non-clear cell ovarian cancer expansion cohort were presented at ASCO 2021 and the initial efficacy data do not support further development in non-clear cell ovarian cancer. The remaining three cohorts, which include non-clear cell endometrial, cervical and clear-cell ovarian and endometrial cancers, showed sufficient responses in stage one of each of the cohorts to advance to stage 2. The data from the cervical cohort have been accepted as a plenary presentation at the Society of Gynecologic Oncology (SGO) 2022 Annual Meeting on Women's Cancer in March 2022 and represent encouraging data in this subset of gynecological cancers. However, given the competing priorities, including development of FAP-2286, we have determined that we will not pursue further development of lucitanib in gynecological cancers at this time.

Competition

The development and commercialization of new drugs is intensely competitive, and we face competition from major pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide. Our competitors may develop or market products or other novel technologies that are more effective, safer or less costly than any that have been or will be commercialized by us, or may obtain regulatory approval for their products more rapidly than we may obtain approval for ours.

The acquisition or licensing of pharmaceutical products is also very competitive. More established companies, which have acknowledged strategies to license or acquire products, may have competitive advantages over us, as may other emerging companies that take similar or different approaches to product acquisitions. Many of our competitors have substantially greater financial, technical and human resources than we have. Our competitors also compete with us in recruiting and retaining qualified scientific, management and commercial personnel as well as in establishing clinical trial sites and patient enrollment for clinical trials.

Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further because of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

Rubraca Competition

Lynparza®/olaparib (AstraZeneca UK Limited) was the first PARP inhibitor to market and has been approved in the US in the following indications:

- for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated ("gBRCAm" or "sBRCAm") advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy;
- in combination with bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with HRD-positive status defined by either:
    - a deleterious or suspected deleterious *BRCA* mutation, and/or
    - genomic instability;
- for the treatment of adult patients who have deleterious or suspected deleterious gBRCAm advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy;
- for the maintenance treatment of adult patients with recurrent epithelial, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy;
- for the treatment of adult patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 ("HER2")-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting;
- for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen; and
- for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair ("HRR") gene-mutated mCRPC who have progressed following prior treatment with enzalutamide or abiraterone.

Lynparza is approved in Europe as monotherapy for the:

- maintenance treatment of adult patients with advanced (FIGO stages III and IV) *BRCA1/2*-mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy;
- maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy;
- treatment of adult patients with germline *BRCA1/2*-mutations, who have HER2 negative locally advanced or metastatic breast cancer. Patients should have previously been treated with an anthracycline and a taxane in the (neo)adjuvant or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor-positive breast cancer should also have progressed on or after prior endocrine therapy, or be considered unsuitable for endocrine therapy;
- for the maintenance treatment of adult patients with germline *BRCA1/2*-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen; and
- for the treatment of adult patients with metastatic castration-resistant prostate cancer and *BRCA1/2*-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent.

Lynparza is approved in Europe in combination with bevacizumab for the:

- maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in combination with bevacizumab and whose cancer is associated with homologous recombination deficiency HRD-positive status defined by either a *BRCA1/2* mutation and/or genomic instability;

AstraZeneca and Merck & Co., Inc. have a global strategic oncology collaboration to co-develop and co-commercialize Lynparza for multiple cancer types. Lynparza is being investigated, alone and in combination with other agents, in multiple indications across several tumor types. Multiple ovarian cancer trials with olaparib in combination with other agents are expecting data read outs in the next 12-24 months in the front-line setting (DUO-O, ENGOT-ov43) and second-line setting (MEDIOLA). In February 2022, positive data from the phase 3 mCRPC trial of olaparib+abiraterone in first line mCRPC were presented at the GU ASCO meeting. Data readouts with olaparib in combination with other agents are also expected in the next 12-24 months in mCRPC (KEYLYNK-010). New olaparib data could impair the relative value of Rubraca in the ovarian cancer and prostate space.

Zejula®/niraparib (GlaxoSmithKline plc) was the first PARP inhibitor approved for maintenance in the recurrent setting and is approved in the United States in the following indications:

- for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy;
- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy; and
- for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with HRD-positive status defined by either:
    - a deleterious or suspected deleterious *BRCA* mutation, or
    - genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy.

Zejula is approved in Europe:

- as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy; and
- as monotherapy for the maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy.

Additional clinical investigations of Zejula in ovarian, breast prostate and lung cancers are ongoing or planned. Janssen Pharmaceuticals has licensed rights to develop and commercialize niraparib specifically for patients with prostate cancer worldwide, except in Japan. Multiple ovarian cancer trials with niraparib in combination with other agents are expected to read out in the next 12-24 months in the front-line setting (FIRST) and the second-line setting (MOONSTONE). Positive data from the MAGNITUDE trial in mCRPC were presented in February 2022 at the GU ASCO meeting. New data for niraparib could impair the relative value of Rubraca in the ovarian and prostate space.

TALZENNA™/talazoparib (Pfizer Inc.) is approved in the US and EU for the treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer. Talazoparib is also being evaluated in the TALAPRO-2 and TALAPRO-3 trials, Phase III studies of enzalutamide plus talazoparib vs. placebo in patients with new mCRPC or HRD associated mCSPC respectively.

There are several PARP inhibitors in clinical development including AbbVie Inc.'s veliparib and ABT-767 and BeiGene, Ltd.'s pamiparib. While most PARP inhibitor development focuses on ovarian, breast and prostate cancers, additional efforts are aimed toward bladder, lung, and pancreatic cancers as well.

Outside of the PARP class, Avastin®/bevacizumab is approved in the US in ovarian cancer for the following indications:

- epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, for Stage III or IV disease following initial surgical resection;

- epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens; and
- epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Avastin as a single agent, for platinum-sensitive recurrent disease.

Additionally, Avastin®/bevacizumab is approved in the EU in ovarian cancer for the following indications:

- in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer;
- in combination with carboplatin and gemcitabine or in combination with carboplatin and paclitaxel, for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents; and
- in combination with paclitaxel, topotecan, or pegylated liposomal doxorubicin is indicated for the treatment of adult patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than two prior chemotherapy regimens and who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor–targeted agents.

Other out-of-class agents approved for use in advanced ovarian cancer include chemotherapeutic agents (e.g. platinum-based doublets, platinum monotherapy, non-platinum chemotherapy, etc.), Doxil® (Janssen Biotech, Inc.), and Hycamtin® (Novartis Pharmaceuticals Corporation). There are additional out-of-class agents in clinical development that may pose a future competitive threat to Rubraca including multiple PD-1 inhibitors alone or in combination with other agents.

FAP-2286 Competition

As of January 2022, there were at least 24 companies in the biopharmaceutical industry developing at least 64 therapeutic or imaging agents that target FAP, including PTRTs, non-peptide-based radionuclide therapies, peptide targeted radionuclide imaging agents, antibody drug conjugate therapies and other FAP-targeted treatment modalities. Of these 64 agents, at least 14 are being developed as FAP-targeted radionuclide therapies. The beta-emitter ^{177}Lu is the primary radioisotope that is being used for therapeutic purposes; however, alpha emitters (e.g., ^{225}Ac) are also being investigated.

Examples of companies who are developing FAP-targeted radionuclide therapies include Novartis, POINT Biopharma, Precision Molecular and Philogen S.p.A. Examples of companies who are developing FAP-targeted radionuclides for imaging applications include SOFIE Biosciences, Lantheus and Noria Therapeutics. Companies are also developing FAP-targeted therapies that do not deliver radiation to solid tumors. These companies include Avacta Life Sciences Ltd, Molecular Partners, AG, Amgen, Roche, PSiOxus Therapeutics, Bioxcel Therapeutics, Oncomatryx Biopharma, Umoja Biopharma and Evotec.

In addition, companies are developing radionuclide therapies that target ligands other than FAP; these therapies may also compete with FAP-2286, especially if they seek to treat the same tumor types that are of interest to Clovis Oncology.

Agents that are approved, widely available, or are established standards of care for treatment of solid tumors that are of interest to us may also be competitive threats to FAP-2286.

Companies developing FAP-targeted radionuclide therapies or imaging agents

- In March 2021, SOFIE Biosciences granted Novartis exclusive worldwide rights to develop and commercialize therapeutic applications for a library of assets that target FAP known as the “FAPI series,” including FAPI-46 and FAPI-74. In addition, the agreement includes co-exclusive rights for Novartis to develop imaging applications for these assets. As of January 2022, neither Novartis nor SOFIE Biosciences have disclosed their clinical development plan for the FAPI series for therapeutic applications.

- POINT Biopharma Global Inc. is developing PNT6555, a D-ala-boroPro based FAP targeting radioligand. POINT Biopharma has disclosed that it intends to develop PNT6555 in multiple tumor types and will commence work on a phase 1 clinical study in 2022. PNT6555 is being combined with an alpha-emitter (^{225}Ac) and beta emitter (^{177}Lu). In addition, POINT Biopharma is supporting the PNT2004 program that is developing other FAP-targeted agents. POINT Biopharma has also entered into an exclusive licensing agreement with Avacta to use its technology (pre|CISION) to develop a range of FAP-activated radiopharmaceuticals, including a prodrug of doxorubicin that is a substrate of FAP.

- Precision Molecular is developing PMI31 to deliver radionuclides for therapeutic applications and PMI07 for imaging applications.

- Philogen S.p.A. is developing OncoFAP, a small molecule ligand with a non-cleavable spacer and DOTAGA chelator attached to various payloads, including radionuclides. OncoFAP-68Ga has been administered in the setting of compassionate use to diagnose cancer patients with advanced solid tumors.

- Lantheus/Noria Therapeutics acquired the exclusive, worldwide rights to develop, manufacture, and commercialize NTI-1309 from Noria Therapeutics in March 2021. NTI-1309 is an imaging agent that targets FAP. In June 2021, Bayer acquired Noria Therapeutics.

In addition to companies who are developing FAP-targeted agents, universities and research institutions are generating data that may inform future development plans of FAP-targeted agents. These institutions and universities include All India Institute of Medical Sciences (developing small molecule FAP inhibitors, including DOTA.SA.FAPi and DOTAGA (SA.FAPi)2), Peking University (developed TEFAPI-06 and TEFAPI-07, both of which are albumin binder-conjugated FAP targeted small molecule inhibitors), Purdue University (developed FAPI-DOTA, a FAP-targeted PI3K inhibitor, FL-L1-TubBH and other FAP-ligand imaging agents), Weill Cornell (developed RPS-309), the Institute of Nuclear Medicine and Allied Science, DRDO (developed FAPI-2DTPA), the University of Minnesota (developed B12 IgG monoclonal antibody) and Radboud University Medical Center Nijmegen (developed 28H1).

Companies developing non-FAP-targeted radionuclide therapies or imaging agents

Endocyte/Novartis - In September 2017, Endocyte, Inc. licensed rights to develop and commercialize agents targeting prostate-specific membrane antigen (PSMA), including the drug candidate 177Lu-PSMA-617. In April 2018, Endocyte initiated VISION, a randomized, open-label phase 3 trial that assessed the efficacy and safety of 177Lu-PSMA-617 with investigator-chosen standard of care versus the best standard of care in the control arm in advanced prostate cancer. In December 2018, Novartis acquired Endocyte, and in March 2021, Novartis announced that the phase 3 VISION trial (NCT03511664) met both primary endpoints, including overall survival and radiographic progression free survival. These data were subsequently published in The New England Journal of Medicine.

In September 2021, the FDA granted Priority Review to 177Lu-PSMA-617 for patients with mCRPC (the Prescription Drug User Fee Act date is anticipated during the first half of 2022). If approved, 177Lu-PSMA-617 has the potential to improve the treatment, diagnosis, or prevention of serious conditions, as determined by the FDA. Novartis will also seek marketing authorization for 177Lu-PSMA-617 using results from the phase 3 VISION trial in Europe.

In addition, other non-FAP targeted radionuclide therapies are in earlier stages of clinical development, including, but not limited to, FPI-2059 (Fusion Pharmaceuticals), FPI-2059, formerly known as IPN-1087 and 3BP-227, targets neurotensin receptor 1. In addition, Bayer is developing three compounds, including BAY2287411 (targets mesothelin), BAY2701439 (targets HER2) and BAY2315497 (targets PSMA).

Companies developing other FAP-targeted therapies that are not linked to radionuclides

In addition to FAP-targeted agents that seek to deliver radionuclides to the body, other FAP-targeted agents that are not linked to radionuclides are being developed.

1. Avacta Life Sciences Ltd. has two therapeutic platforms (pre|CISION and TMAC, short for "tumor microenvironment activated drug conjugates") that are being used to target FAP and other ligands. The pre|CISION platform can be used to generate prodrug forms of chemotherapeutic agents that are inactive in the circulation. The TMAC platform is being used to design activated drug conjugates to help concentrate the delivery of chemotoxins to the tumor microenvironment.

   AVA6000 is an FAP activated doxorubicin prodrug that is using the pre|CISION platform. AVA6000 binds to and is cleaved by FAP in the tumor microenvironment to deliver active doxorubicin to the tumor. At least one clinical trial (NCT04969835) is evaluating the safety, pharmacokinetics, and efficacy of AVA6000 in solid tumors.

2. Molecular Partners, AG, in collaboration with Amgen, is developing MP0310 (also known as AMG506), a multi-specific FAP x 4-1BB-targeting DARPin® drug candidate. MP0310 (AMG 506) is designed to activate immune cells in the tumor and not in the rest of the body. MP0310 (AMG 506) is being investigated in at least one clinical trial (NCT04049903) in patients with advanced solid tumors.

   In addition, Molecular Partners is developing MP0317, a DARPin drug candidate targeting FAP and CD40. MP0317 is being investigated in at least one clinical trial (NCT05098405) in patients with advanced solid tumors. Molecular Partners AG has disclosed that results from this clinical trial should be available during the second half of 2022.

   In December 2021, Molecular Partners disclosed that it is collaborating with Novartis to develop a DARPin-conjugated radioligand therapy that targets specific tumor-associated antigens. Novartis will be responsible for the clinical development and commercialization of the radioligand therapy.

3. Roche is developing several FAP-targeted agents, including RO7122290 (also known as RG7827) and RO7300490 (also known as RG6189). RG7827 is a bispecific monoclonal antibody linked to 4-1BB ligand that targets FAP. RG6189 is also a bispecific monoclonal antibody liked to CD40 that is also targeting FAP.

   Two clinical trials for RO7122290/RG7827 include a phase 1b trial (NCT04826003) that is investigating RO7122290 in combination with cibisatamab after pretreatment with obinutuzumab in participants with previously treated metastatic, microsatellite-stable colorectal adenocarcinoma with high CEACAM5 expression, and a phase 1b/2 umbrella study (NCT03869190) investigating single-agent RG7827 and RG7827 in combination with atezolizumab in patients with muscle invasive bladder cancer and in participants with locally advanced or metastatic urothelial carcinoma who have progressed during or following a platinum-containing regimen.

   In one phase 1 trial (NCT04857138), RO7300490 is being evaluated for safety, pharmacokinetics, and anti-tumor activity as a single agent or in combination with atezolizumab in patients with solid tumors.

   Although Roche was developing two additional FAP-targeted agents (RG7461/RO6874281 and RG7386/RO6874813), Roche announced that it has discontinued development of both agents.

4. PSIOxus Therapeutics is developing an oncolytic adenoviral vector (NG-641) designed to deliver genes to tumor cells that produce proteins targeting tumor-associated stromal fibroblasts. The NG-641 virus encodes genes for FAP-targeting bispecific T-cell activator (FAP-TAc), the chemokines CXCL9 and CXCL10, and interferon alpha. As of January 2022, there were three clinical trials for NG-641 listed on ClinicalTrials.gov.

5. Bioxcel Therapeutics is developing talabostat (BXCL701), a molecule that is designed to inhibit dipeptidyl peptidase (DPP) 8/9 and block immune evasion by targeting FAP. As of January 2022, there were 12 clinical trials for talabostat (BXCL701) listed on ClinicalTrials.gov.

6. Oncomatryx Biopharma SL is developing OMTX705, an anti-FAP antibody drug conjugate that is conjugated to cytolysin. In vivo, OMTX705 led to 100% tumor growth inhabitation as a single agent and tumor regression when combined with gemcitabine and/or paclitaxel. As of January 13, 2022, there were no clinical trials for OMTX705 listed on ClinicalTrials.gov.

7. Umoja Biopharma is developing UB-TT500 to target FAP. TT500 uses Umoja Biopharma's "TumorTags" technology. TumorTag enables binding of a molecule to cancer cells and "tags" them as targets for CAR-T cells.

8. Evotec is developing a small molecule FAP inhibitor; however, Evotec seeks to out-license its technology to a partner.

Lucitanib Competition

Competitive threats to lucitanib in gynecological cancers (primarily endometrial and cervical) include other kinase inhibitors and checkpoint inhibitors.

Eisai and Merck have established a strategic collaboration for the worldwide co-development and co-commercialization of Lenvima (lenvatinib), a kinase inhibitor, including endometrial cancers. Lenvima is currently in a phase III in combination with pembrolizumab for the first-line treatment of advanced or recurrent endometrial carcinoma (LEAP-001). Lenvima is currently approved for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high or mismatch repair deficient, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.

In cervical cancer, the recent approval of several drugs and combinations have changed the treatment landscape for this cancer. In front line metastatic setting pembrolizumab with chemotherapy and bevacizumab was approved with a significant survival advantage over chemotherapy and bevacizumab. SeaGen also received FDA approval for tisotumab vedotin (ADC targeting tissue factor) in the relapsed metastatic setting for cervical cancer, and Regeneron's cemiplimab (PD-1 inhibitor) has also been accepted for priority review by the FDA with a decision in January 2022.

License Agreements

Pfizer Inc.

In June 2011, we entered into a license agreement with Pfizer, Inc. ("Pfizer") to obtain the exclusive global rights to develop and commercialize Rubraca. The exclusive rights are exclusive even as to Pfizer and include the right to grant sublicenses. Pursuant to the terms of the license agreement, we made a $7.0 million upfront payment to Pfizer and are required to make additional payments to Pfizer for the achievement of certain development and regulatory and sales milestones and royalties on sales as required by the license agreement. Prior to the FDA approval of Rubraca, we made milestone payments of $1.4 million, which were recognized as acquired in-process research and development expense.

During 2016 through 2020, we paid Pfizer a total of $82.5 million in milestone payments related to FDA and European Commission approvals received for Rubraca. These milestone payments were recognized as intangible assets and are amortized over the estimated remaining useful life of Rubraca.

We are obligated under the license agreement to use commercially reasonable efforts to develop and commercialize Rubraca and we are responsible for all ongoing development and commercialization costs for Rubraca. We are required to make regulatory milestone payments to Pfizer of up to an additional $8.0 million in aggregate if specified clinical study objectives and regulatory filings, acceptances and approvals are achieved. In addition, we are obligated to make sales milestone payments to Pfizer if specified annual sales targets for Rubraca are met, which relate to annual sales targets of $250.0 million and above, which, in the aggregate, could amount to total milestone payments of $170.0 million, and tiered royalty payments at a mid-teen percentage rate on net sales, with standard provisions for royalty offsets to the extent we need to obtain any rights from third parties to commercialize Rubraca.

The license agreement with Pfizer will remain in effect until the expiration of all of our royalty and sublicense revenue obligations to Pfizer, determined on a product-by-product and country-by-country basis, unless we elect to terminate the license agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, Pfizer can terminate the agreement, resulting in a loss of our rights to Rubraca and an obligation to assign or license to Pfizer any intellectual property rights or other rights we may have in Rubraca, including our regulatory filings, regulatory approvals, patents and trademarks for Rubraca.

AstraZeneca UK Limited

In April 2012, we entered into a license agreement with AstraZeneca UK Limited ("AstraZeneca") to acquire exclusive rights associated with Rubraca under a family of patents and patent applications that claim methods of treating patients with PARP inhibitors in certain indications. The license enables the development and commercialization of Rubraca for the uses claimed by these patents. AstraZeneca also receives royalties on net sales of Rubraca.

3B Pharmaceuticals GmbH ("3BP")

In September 2019, we entered into a global license and collaboration agreement with 3BP to develop and commercialize a PTRT and imaging agent targeting FAP. The lead candidate, designated internally as FAP-2286, is being developed pursuant to a global development plan agreed to by the parties. We are responsible for the costs of all preclinical and clinical development activities described in the plan, including the costs for a limited number of 3BP full-time equivalents and external costs incurred during the preclinical development phase of the collaboration. Upon the signing of the license and collaboration agreement in September 2019, we made a $9.4 million upfront payment to 3BP, which we recognized as acquired in-process research and development expense.

Pursuant to the terms of the FAP agreement, we are required to make additional payments to 3BP for annual technology access fees and upon the achievement of certain development and regulatory milestone events (or on certain dates, whichever occur earlier). We are also obligated to pay 3BP single- to low-double-digit royalties on net sales of the FAP-targeted therapeutic product and imaging agent, based on the volume of annual net sales achieved. In addition, 3BP is entitled to receive 34% of any consideration, excluding royalties on the therapeutic product, pursuant to any sublicenses we may grant.

We are obligated under the license and collaboration agreement to use diligent efforts to develop FAP-2286 and commercialize a FAP-targeted therapeutic product and imaging agent, and we are responsible for all commercialization costs in our territory. The agreement with 3BP will remain in effect until the expiration of our royalty obligations to 3BP, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, 3BP can terminate the agreement, resulting in a loss of our rights. 3BP also has the right to terminate the agreement under certain circumstances in connection with our change of control in which the acquiring party retains a product competitive with the FAP-targeted therapeutic product or, in the event marketing authorization has not yet been obtained, does not agree to the then-current global development plan.

We submitted two INDs for FAP-2286 for use as imaging and treatment agents in December 2020 to support an initial phase 1 study to determine the dose and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development program. In April 2021, we made a milestone payment to 3BP under the license and collaboration agreement of $2.2 million as a result of the FDA's acceptance of the IND for the treatment agent. In September 2021, we made a milestone payment to 3BP under the license and collaboration agreement of $3.3 million as a result of the initiation of our LuMIERE Phase 1/2 study.

In February 2020, we finalized the terms of a drug discovery collaboration agreement with 3BP to identify up to three additional, undisclosed targets for PTRT, to which we will obtain global rights for any resulting product candidates. We are responsible for the costs of all preclinical and clinical development activities conducted under the discovery program, including the costs for a limited number of 3BP full-time equivalents and external costs incurred during the discovery and preclinical development phase for each collaboration target. The discovery collaboration agreement was effective December 31, 2019, for which we incurred a $2.1 million technology access fee, which we accrued and recognized as a research and development expense.

Pursuant to the terms of the discovery collaboration agreement, we are required to make additional payments to 3BP for annual technology access fees and upon the achievement of certain development and regulatory milestone events (or on certain dates, whichever occur earlier). We are also obligated to pay 3BP a 6% royalty on net sales of License Products (as defined in the agreement), based on the volume of quarterly net sales achieved.

We are obligated under the discovery collaboration agreement to use diligent efforts to develop and commercialize the product candidates, if any, that result from the discovery program, and we are responsible for all clinical development and commercialization costs. The agreement with 3BP will remain in effect until the expiration of our

royalty obligations to 3BP, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, 3BP can terminate the agreement, resulting in a loss of our rights.

Advenchen Laboratories LLC

On November 19, 2013, we acquired all of the issued and outstanding capital stock of EOS pursuant to the terms set forth in that certain Stock Purchase Agreement, dated as of November 19, 2013 (the "Stock Purchase Agreement"), by and among the Company, EOS, its shareholders (the "Sellers") and Sofinnova Capital V FCPR, acting in its capacity as the Sellers' representative. Following the acquisition, EOS became a wholly-owned subsidiary of the Company. Under the terms of the Stock Purchase Agreement, in addition to the initial purchase price paid at the time of the closing of the acquisition and other license fees due to Advenchen described below, we will also be obligated to pay to the Sellers a milestone payment of $65.0 million upon obtaining the first NDA approval from the FDA with respect to lucitanib.

In October 2008, Ethical Oncology Science, S.p.A. ("EOS") (now known as Clovis Oncology Italy Srl) entered into an exclusive license agreement with Advenchen Laboratories LLC ("Advenchen") to develop and commercialize lucitanib on a global basis, excluding China.

We are obligated to pay Advenchen tiered royalties at percentage rates in the mid-single digits on net sales of lucitanib, based on the volume of annual net sales achieved. In addition, after giving effect to the first and second amendments to the license agreement, we are required to pay to Advenchen 25% of any consideration, excluding royalties, we receive from sublicensees, in lieu of the milestone obligations set forth in the agreement. We are obligated under the agreement to use commercially reasonable efforts to develop and commercialize at least one product containing lucitanib, and we are also responsible for all remaining development and commercialization costs for lucitanib.

The license agreement with Advenchen will remain in effect until the expiration of all of our royalty obligations to Advenchen, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, Advenchen can terminate the agreement, resulting in a loss of our rights to lucitanib.

Government Regulation

Government authorities in the United States (including federal, state and local authorities) and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, pricing and export and import of pharmaceutical products such as Rubraca and our other product candidates. Our product candidates must be approved by the FDA through the NDA process before they may be legally placed on the market in the United States. In the European Union, a product requires approval from the European Commission ("EC") following a favorable assessment from the European Medicines Agency ("EMA") through the marketing authorization application ("MAA") process for a product falling within the scope of the centralized procedure or a national MAA process (albeit through mutual recognition or decentralized procedure). Our product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Moreover, failure to comply with applicable regulatory requirements may result in, among other things, warning letters, clinical holds, civil or criminal penalties, recall or seizure of products, injunction, disbarment, partial or total suspension of production or withdrawal of the product from the market.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive non-clinical laboratory tests (evaluations of product chemistry, toxicity and formulation) and non-clinical animal studies, all performed in accordance with the FDA's Good Laboratory Practice regulations;

- submission to the FDA of an IND which must become effective before human clinical trials may begin and must be updated at least annually;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication;
- submission to the FDA of a marketing authorization application in the form of an NDA for the initial commercial sale of a product, or of a sNDA, for approval of a new indication if the product is already approved for another indication;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the active pharmaceutical ingredient ("API") and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices ("cGMP") and/or sites involved in clinical studies to assess compliance with Good Clinical Practices ("GCP");
- if FDA convenes an advisory committee, satisfactory completion of the advisory committee review; and
- FDA review and approval of the marketing authorization application and product prescribing information prior to any commercial marketing or sale of the drug for the intended use.

An IND is a request for authorization from the FDA to administer a product candidate to humans for further research of the drug candidate's safety and/or efficacy. The central focus of an IND submission is on the general investigational plan for the drug candidate and the protocol(s) for human studies. The IND also includes results of animal studies or other human studies, as appropriate, as well as manufacturing information, analytical data and any available clinical data or literature to support the use of the product candidate. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND may be placed on clinical hold requiring delay of a proposed clinical investigation, and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the drug candidate to human subjects under the supervision of qualified investigators and in accordance with GCP, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from an Institutional Review Board ("IRB") for each medical center proposing to conduct the clinical trial before the trials may be initiated, and the IRB must monitor the study until completed. Clinical trials are subject to central registration and results reporting requirements, such as on www.clinicaltrials.gov.

The clinical investigation of a product candidate is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases of an investigation are as follows:

- Phase 1. Phase 1 includes the initial introduction of the product candidate into humans. Phase 1 clinical trials are typically closely monitored and may be conducted in patients with the target disease or condition or in healthy volunteers. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of product candidate in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the product candidate's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials. The total number of participants included in Phase 1 clinical trials varies but is generally in the range of 20 to 80.
- Phase 2. Phase 2 includes controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the product candidate for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population, usually involving no more than several hundred participants.

- Phase 3. Phase 3 clinical trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug product and to provide an adequate basis for product approval. Phase 3 clinical trials usually involve several hundred to several thousand participants.

A pivotal study is a clinical study which adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are also Phase 3 studies but may be Phase 2 studies if the trial design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need.

Human clinical trials are inherently uncertain, and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA, an IRB or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as an Independent Data Monitoring Committee ("IDMC"). The IDMC receives special access to un-blinded data during the clinical trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed product development information is submitted to the FDA in the form of an NDA or sNDA requesting approval to market the product for one or more indications.

The application includes all relevant data available from pertinent non-clinical and clinical trials, including negative or ambiguous results, as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the product candidate to the satisfaction of the FDA.

Once the marketing application submission has been accepted for filing, the FDA's goal is to review applications within 10 months of acceptance for filing or, if the sponsor has been granted priority review designation, on the basis of an improvement in the treatments of a serious condition, six months from acceptance for filing. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations.

After the FDA evaluates the NDA or sNDA and conducts inspections of clinical research facilities and/or manufacturing facilities where the drug product and/or its API will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, non-clinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the application does not satisfy the criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategies plan to mitigate risks, which could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase IV clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug.

Products manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences with the drug. Adverse event experience with the product must be reported to the FDA in a timely fashion and pharmacovigilance programs to proactively look for these adverse events are mandated by the FDA. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications and also may require the implementation of other risk management measures.

Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for quality and compliance, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Following such inspections, the FDA may issue notices on Form FDA 483 and Warning Letters that could cause us to modify certain activities. A Form FDA 483 notice, if issued at the conclusion of an FDA inspection, can list conditions the FDA investigators believe may have violated cGMP or other FDA regulations or guidance. Failure to adequately and promptly correct the observations(s) can result in further regulatory enforcement action. In addition to Form FDA 483 notices and Warning Letters, failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Government Regulation Outside of the United States

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country, and the time may be longer or shorter than that required for FDA approval.

Regardless of whether we hold FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, ("CTA") must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

Medicines can be authorized in the EU by using either the centralized authorization procedure or national authorization procedures. Under the centralized procedure, marketing authorization applications are submitted to the EMA whose CHMP reviews the application and issues an opinion on it. The opinion is considered by the EC which is responsible for deciding applications. If the application is approved, the EC grants a single marketing authorization that is valid for all EU member states as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human medicines that contain a new active substance indicated for the treatment of certain diseases, including cancer.

The national authorization procedures, the decentralized and mutual recognition procedures, are available for products for which the centralized procedure is not compulsory. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure. Under the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

As result of the United Kingdom ("UK") leaving the EU, the UK is no longer part of the harmonized EU medicines network. The UK government introduced legislation to allow the continued registration, sale and access to medicinal

products including regulation to allow implementation of the Northern Ireland Protocol. A comprehensive national regime for the authorization of medicinal products for human use; for the manufacture, import, distribution, sale and supply of those products; for their labelling and advertising; and for pharmacovigilance have been introduced. In Northern Ireland the, EU regulations will continue to apply in accordance with the Northern Ireland Protocol.

Available Special Regulatory Procedures

Formal Meetings

We are encouraged to engage and seek guidance from health authorities relating to the development and review of investigational drugs, as well as marketing applications. In the United States, there are different types of official meetings that may occur between us and the FDA. Each meeting type is subject to different procedures. Conclusions and agreements from each of these meetings are captured in the official final meeting minutes issued by the FDA.

The EMA also provides the opportunity for dialogue with us. This is usually done in the form of Scientific Advice, which is given by the Scientific Advice Working Party of CHMP. A fee is incurred with each Scientific Advice meeting.

Advice from either the FDA or EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies and pharmacovigilance plans and risk-management programs. Such advice is not legally binding on the sponsor. To obtain binding commitments from the FDA in the United States, Special Protocol Assessment ("SPA") procedures are available. A SPA is an evaluation by the FDA of a protocol with the goal of reaching an agreement with the sponsor that the protocol design, clinical endpoints and statistical analyses are acceptable to support regulatory approval of the product candidate with respect to effectiveness in the indication studied. The FDA's agreement to a SPA is binding upon the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining the safety or effectiveness of the product after clinical studies begin, or if the study sponsor fails to follow the protocol that was agreed upon with the FDA. There is no guarantee that a study will ultimately be adequate to support an approval even if the study is subject to a SPA.

Orphan Drug Designation

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States. In the EU, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the EU Community. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

In Europe, orphan drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Pediatric Development

In the United States, the FDCA provides for an additional six months of marketing exclusivity for a drug if reports are filed of investigations studying the use of the drug product in a pediatric population in response to a written request from the FDA. Separate from this potential exclusivity benefit, NDAs must contain data (or a proposal for post-marketing activity) to assess the safety and effectiveness of an investigational drug product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-Phase II meeting and submission of the NDA.

For the EMA, a Pediatric Investigation Plan, and/or a request for waiver or deferral, has to be agreed prior to submitting an initial marketing authorization application and prior to submitting a variation to an existing Marketing Authorization to add an additional indication.

Breakthrough Therapy Designation in the United States

The U.S. Congress created the Breakthrough Therapy designation program as a result of the passage of the Food and Drug Administration Safety and Innovation Act of 2012. FDA may grant Breakthrough Therapy status to a drug intended for the treatment of a serious condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The Breakthrough Therapy designation, which may be requested by a sponsor when filing or amending an IND, is intended to facilitate and expedite the development and FDA review of a product candidate. Specifically, the Breakthrough Therapy designation may entitle the sponsor to more frequent meetings with the FDA during drug development, intensive guidance on clinical trial design and expedited FDA review by a cross-disciplinary team comprised of senior managers. The designation does not guarantee a faster development or review time as compared to other drugs, however, nor does it assure that the drug will obtain ultimate marketing approval by the FDA. Once granted, the FDA may withdraw this designation at any time.

Expedited Review and Approval in the United States

The FDA has various programs, including Fast Track, priority review and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs and biologics, and/or provide for the approval of a drug or biologic on the basis of a surrogate endpoint. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, based on results of the Phase 3 clinical trial(s) submitted in an NDA, upon the request of an applicant, the FDA may grant the NDA a priority review designation, which sets the target date for FDA action on the application at six months from the 60-day filing date, if the drug is a new molecular entity, rather than to the standard FDA review period of 10 months. Priority review is granted where preliminary estimates indicate that a product, if approved, has the potential to provide a safe and effective therapy where no satisfactory alternative therapy exists, or a significant improvement compared to marketed products is possible. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Fast Track is a designation which is more similar to the Breakthrough Therapy designation, but is granted based on preliminary data including non-clinical or mechanistic data, and allows more frequent communication with FDA to expedite drug development

Accelerated approval provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit and is better than available therapy. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. The FDA will also consider the severity, rarity or prevalence of the condition. As a condition of approval for drugs granted accelerated approval, one or more post-marketing confirmatory studies are required to confirm as

predicted by the surrogate marker trial an effect on clinical benefit, which is defined as having a positive effect on how a patient feels, functions or survives.

Accelerated Review in the European Union

Under the Centralized Procedure in the EU, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, defined by three cumulative criteria: the seriousness of the disease (e.g. heavy disabling or life-threatening diseases) to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days of submission of the MAA, excluding clock stops.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of Rubraca and any other drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of approved pharmaceutical products depend in part on the availability of reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, public and private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved or European Commission/specific country-approved drugs for a particular indication (or all indications for an approved drug). Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services and imposing controls to manage costs. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost effectiveness of our products, in addition to the costs required to obtain approvals. In any event, our approved products may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be established. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Third-party payors impose price protection in their contracts with manufacturers to limit the manufacturer's ability to increase price in exchange of providing equal access to the drug product vs. other competing drugs.

The prescription drug benefit administered by the United States government provides it with certain cost containment tools. The Medicare Part D prescription drug benefit works as a public sector-private sector partnership, whereby Medicare Part D prescription drug plans receive funding from the Federal Medicare program, which they use to pay pharmacies for drugs dispensed to Medicare Part D enrollees. The Part D prescription drug plans seek to contain costs by contracting with manufacturers which pay rebates in exchange for favorable formulary placement. Anti-cancer agents currently have guaranteed favorable status on these formularies, but the Medicare program can remove that status, which would result in higher rebate payments. Even with the current, guaranteed favorable formulary placement, we must still pay some portion of patient expenses when they enter into the coverage gap period referred to as the "donut hole." We participate in this Medicare Part D Coverage Gap Discount Program because it is a precondition to Medicare Part D coverage for our products.

There is some uncertainty as to our arrangements with commercial pharmacy benefit managers ("PBMs") and Medicare Part D prescription drug plans, going forward. In November 2020, the Department of Health and Human Services Office of Inspector General (OIG) issued a Final Rule that would, effective January 1, 2026, eliminate the Anti-Kickback Statute safe harbor for rebates paid to Medicare Part D plans or to PBMs on behalf of such plans. While we cannot anticipate the effects of this change to the way it currently contracts, this new framework could significantly alter the way it does business with Part D plan sponsors and PBMs on behalf of such plans. This rulemaking also established, effective January 1, 2021, a new safe harbor for point-of-sale discounts at the pharmacy counter and a new safe harbor for certain services arrangements between pharmaceutical manufacturers and PBMs. Most of our current contracts do not meet the requirements that will go into effect in 2026. We may incur costs renegotiating these agreements, and their terms may be less favorable.

The US Federal government is continuing to seek other cost containment tools. In legislation that had previously been introduced in 2021 as part of the Build Back Better Act (the "BBBA"), there were provisions that would have allowed the Federal government to negotiate prices for some high-cost drugs covered under Medicare Parts A and B. More broadly, all drugs would have been subject to inflation penalties if their costs rise faster than inflation. Although the BBBA has not passed, some portions of the bill are likely to be included in other laws that may be more successful.

Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that federal, state and local governments in the United States will continue to consider legislation to limit the growth of healthcare costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as our products.

The marketability of any products for which we receive regulatory approval for commercial sale may be subject to the impact that government and third-party coverage and reimbursement decisions have on patients. Increasing coinsurance responsibilities can dissuade patients from receiving medications, including our products. To offset the impact of coinsurance on patient adherence, we offer copay assistance to patients not covered by United States federal healthcare programs. However, the Medicare program has implemented a new rule that would cause a significant increase in our rebates to state Medicaid programs resulting from the continued provision of copay assistance to patients. That rule takes effect on January 1, 2023, unless a lawsuit by PhRMA against the Medicare program is successful. We may need to evaluate offering coinsurance support if the rule goes into effect, which would be very detrimental to medication adherence.

Different pricing and reimbursement schemes exist in other countries and vary widely from country to country. In Europe, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund the cost of those products to consumers. These jurisdictions operate a system under which products may only be marketed once a reimbursement price has been agreed for a defined population that, depending on country-specific negotiations, could be equal to European Commission-granted indication or a restricted population. To obtain reimbursement and pricing approval in Europe, some of these European countries may require additional economic evidence, referred to as a health technology assessment (HTA). In European countries, repeating price/reimbursement negotiations take place depending on local healthcare situations and can lead to lower reimbursed prices over time.

The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasing high barriers are being erected to the entry of new products. In addition, in some countries, especially in Europe, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. In particular, for each new indication, new negotiations are required to obtain reimbursement in European countries; also, pricing negotiations in European countries are often linked to baskets of comparator countries; due to Brexit, it is currently unclear whether changes in country baskets will take place anytime soon. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in Europe do not follow price structures of the United States and generally prices tend to be significantly lower. Additionally, European Union competition laws allow the parallel importation of branded drugs between member countries. This allows buyers in countries where government-approved prices for Rubraca are relatively high to purchase it from countries where the prices for Rubraca are relatively low. Purchases of Rubraca in countries where our selling prices are relatively low for resale in countries in which our selling prices are relatively high may impact our overall margins on Rubraca and thereby negatively affect our earnings.

Coverage policies and third-party reimbursement rates may change at any time in the United States and Europe. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Advertising and Promotion

The FDA and other U.S. federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, the FDCA and the FDA's implementing regulations and standards. The FDA's review of marketing and promotional activities encompasses, but is not limited to, direct-to-consumer advertising, healthcare provider-directed advertising and promotion, sales representative communications to healthcare professionals, communications regarding unapproved or "off-label" uses, industry sponsored scientific and educational activities, and promotional activities involving the internet. A product cannot be commercially promoted before it is approved. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by the FDA. FDA regulations also impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements and restrictions regarding unapproved uses of a drug or for other violations of its advertising and labeling laws and regulations, may result in adverse publicity and enforcement action by the FDA, the Department of Justice or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. A range of penalties are possible that could have significant commercial consequences, including product seizures, injunctions, administrative remedies, civil and/or criminal fines, agreements that materially restrict the manner in which a company promotes or distributes its products, or regulatory enforcement letters which may require corrective advertising or other corrective communications to healthcare professionals or consumers.

Other Healthcare Laws and Compliance Requirements

We are subject to various laws targeting fraud and abuse in the healthcare industry, including federal and state anti-kickback laws and false-claims laws. Violations of these laws can lead to civil and criminal penalties, including fines, imprisonment and administrative remedies such as exclusion from participation in federal healthcare programs.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as Medicare and Medicaid. The reach of the Anti-Kickback Statute was broadened by the Affordable Care Act, which, among other things, amended the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim submitted in violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal civil False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal program, including federal healthcare programs. The "qui tam" provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payor and not merely a federal healthcare program. When an entity is determined to have violated the federal False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil fines and penalties.

In addition, a person who offers or transfers to a Medicare or Medicaid beneficiary any remuneration, including waivers of co-payments and deductible amounts (or any part thereof), that the person knows or should know is likely to influence the beneficiary's selection of a particular provider, practitioner or supplier of Medicare or Medicaid-payable items or services, may be liable for civil monetary penalties of up to $20,000 for each wrongful act. Moreover, in certain cases, providers who routinely waive copayments and deductibles for Medicare and Medicaid beneficiaries can also be held liable under the federal Anti-kickback Statute and False Claims Act, which can impose additional penalties. One of the statutory exceptions to this prohibition is non-routine, unadvertised waivers of copayments or deductible amounts based on individualized determinations of financial need or exhaustion of reasonable collection efforts. The Office of Inspector General of the Department of Health and Human Services emphasizes, however, that this exception should

only be used occasionally to address special financial needs of a particular patient. Although this prohibition applies only to federal healthcare program beneficiaries, the routine waivers of copayments and deductibles offered to patients covered by commercial payers may implicate applicable state laws related to, among other things, unlawful schemes to defraud, excessive fees for services, tortious interference with patient contracts and statutory or common law fraud. To the extent our patient assistance programs are found to be inconsistent with applicable laws, we may be required to restructure or discontinue such programs or be subject to significant penalties.

In addition to the laws described above, drug manufacturers must report to CMS payments made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information to CMS may result in civil monetary penalties of up to an aggregate of $178,581 per year (or up to an aggregate of $1.190 million per year for "knowing failures"), adjusted for inflation, for all payments, transfers of value, or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Applicable drug manufacturers are required to collect data for each calendar year and submit reports to CMS by March 31st of each subsequent calendar year. In addition, there is also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. These laws impose administrative and compliance burdens that may affect our sales, marketing, and other promotional activities.

For marketed products which are covered in the United States by the Medicaid program, we have various obligations, including government price calculation and reporting and rebate requirements which generally require products be offered at substantial rebates/discounts to Medicaid and certain purchasers (including "covered entities" purchasing under the 340B Drug Discount Program). We are also required to discount such products to authorized users of the Federal Supply Schedule of the General Services Administration, under which additional laws and requirements apply. These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the execution of government procurement contracts governed by the Federal Acquisition Regulations. The guidance governing such calculations is not always clear and may require significant investment in personnel, systems and resources in order to comply. Failure to properly calculate our prices, or offer required discounts or rebates could subject us to substantial penalties.

One component of the rebate and discount calculations under the Medicaid and 340B programs is the "additional rebate", a complex calculation which is based, in part, on the rate at which a branded drug's price increases over time as compared to the rate of inflation (based on the CPI-U published by the United States Department of Labor). This calculation is based on the baseline pricing data for the first full quarter of sales associated with a branded drug's NDA, and baseline data cannot generally be reset, even on transfer of the NDA to another manufacturer. This "additional rebate" calculation can, in some cases where price increases have been relatively high versus the first quarter of sales of the NDA, result in Medicaid rebates up to 100% of a drug's "average manufacturer price" and 340B prices of one penny. Separately, subject to the control of Directive 89/105/EEC, pricing and reimbursement in the EU/EEA ("European Economic Area") is governed by national rules and policies and may vary from Member State to Member State.

Also, the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") outlines several federal crimes, including health care fraud and false statements relating to health care matters. Most healthcare providers who are expected to prescribe our products and from whom we obtain patient health information are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The privacy and protection of consumer information remains a developing area and we continue to monitor legislative and regulatory developments both in the United States as well as Europe. For example, the California Consumer Privacy Act ("CCPA") became effective on January 1, 2020 and, as enacted, requires us to make new disclosures to consumers about our data collection, use, and sharing practices. It also provides a cause of action for data breaches. Beyond California, many other states are developing their own data privacy protections, which, along with the CCPA, could create liability for us or increase our cost of doing business. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. For example, the General Data Protection Regulation (Regulation (EU) 2016/679), the U.K.'s Data Protection Act 2018 and the Swiss Federal Data Protection Act and Data Protection Ordinance, regulate the processing of personal data within the U.K., the EU and between countries in the EU, U.K. and countries outside of the EU and U.K., including the U.S. Failure to provide adequate privacy protections and maintain compliance with the EU, U.K. and Swiss Privacy Laws, could jeopardize business transactions

across borders and result in significant penalties. Similar to the impact of the CCPA or other U.S. state frameworks, these European laws could create liability for us or increase our cost of doing business.

Regulation of Diagnostic Tests

In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, non-clinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Diagnostic tests are classified as medical devices under the FDCA. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution, depending on their classification by FDA.

In the United States, devices are classified into one of three classes (Class I, II, or III) based on the controls deemed necessary by the FDA to reasonably ensure their safety and effectiveness. Class I and II devices are subject to general controls including, but not limited to, performance standards, premarket notification, also called 510(k) clearance, and post market surveillance. Class III devices are those that either support or sustains human life, are of substantial importance in preventing impairment of human health, or present a potential, unreasonable risk of illness or injury. Class III devices are subject to more rigorous review and approval requirements than Class I or II, known as a premarket approval, or PMA approval. Because the diagnostic tests being developed by our third-party collaborators are of substantial importance in preventing impairment of human health, they are considered Class III devices, subject to the PMA approval process.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, non-clinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. FDA review of an initial PMA application is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards is not maintained, or problems are identified following initial marketing.

We and our third-party collaborators who are developing companion diagnostics work cooperatively to generate the data required for submission with a PMA application and the diagnostic partner is responsible for maintaining close contact with the Center for Devices and Radiological Health ("CDRH") at the FDA to ensure that any changes in requirements are incorporated into the development plans. Meetings with the FDA with regard to our drug product candidates, as well as companion diagnostic product candidates, typically include representatives from the Center for Drug Evaluation and Research and CDRH when appropriate to ensure that the NDA and PMA submissions are coordinated to enable FDA to conduct a parallel review of both submissions. The FDA has issued guidance documents addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to these guidance documents, for novel therapeutic products such as our product candidates, the PMA for a companion diagnostic device should generally be developed and approved or cleared contemporaneously with the therapeutic. In order to achieve this, the diagnostic may be subject to post approval study requirements.

In the EU, Regulation EU 2017/746 introduced substantial changes to the regulatory framework for In-Vitro Diagnostics starting on May 26, 2022. The regulation introduces certain requirements for In Vitro Diagnostics and a stronger role for so-called conformity assessment bodies. Conformity assessment bodies (so-called 'notified bodies') will independently monitor whether devices comply with the safety and performance requirements before they reach the EU market. In order to prevent disruption of supply of essential healthcare products, especially in the context of the COVID-

19 pandemic, the European Commission agreed a progressive roll-out of the regulation. The date of application of some aspects of the regulation requirements has been amended according to the risk category of the device.

No change is proposed for CE-marked devices that do not require notified body involvement under the IVD Regulation, or for devices that are "new" (i.e., devices that have neither a notified body certificate nor a declaration of conformity under the current Directive 98/79/EC). For those types of devices, the IVD Regulation will apply starting on May 26, 2022. The data generated for the U.S. PMA registration will likely be sufficient to satisfy the regulatory requirements for the EU and other countries.

Patents and Proprietary Rights

The proprietary nature of, and protection for, our product candidates, technology and know-how are important to our business. Our success depends in part on our ability to protect the proprietary nature of our product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek patent protection in the United States and internationally for our product candidates and other technology. Our policy is to patent or in-license the technology, inventions and improvements that we consider important to the development of our business. We also rely on trade secrets, know-how and continuing innovation to develop and maintain our competitive position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology.

In June 2011, we obtained an exclusive, worldwide license from Pfizer to develop and commercialize rucaparib. In April 2012, we obtained an exclusive license from AstraZeneca under a family of patents and patent applications which permits the development and commercialization of rucaparib for certain methods of treating patients with PARP inhibitors.

We were granted patent term extension to November 22, 2023 under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act") for U.S. Patent 6,495,541 directed to the rucaparib composition of matter. Additionally, other patents and patent applications are directed to methods of making, methods of using, dosing regimens, various salt and polymorphic forms, and formulations with expiration dates through potentially 2035. These patents and patent applications include the rucaparib camsylate salt/polymorph patent family licensed from Pfizer, which expires in 2031, and a patent family directed to high dosage strength rucaparib tablets, which expires in 2035. To date, the rucaparib camsylate salt/polymorph patents issued in 53 jurisdictions (including the United States and Europe), with applications pending in 4 jurisdictions. Patents directed to the high dosage strength rucaparib tablets, including all commercial dosage strengths, issued in the United States and 6 other jurisdictions, and applications are pending in 12 jurisdictions, including before the European Patent Office. United States patents with claims that cover Rubraca and its uses are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book.

Because Rubraca does not contain a previously approved active ingredient, the Hatch-Waxman Act provides a five-year period of new chemical entity ("NCE") exclusivity following its December 19, 2016 approval during which time generic competitors cannot file an Abbreviated New Drug Application ("ANDA") for a generic version of Rubraca, unless the submission contains a Paragraph IV Certification that one or more patents listed in the Orange Book for Rubraca are invalid, unenforceable or will not be infringed by a proposed ANDA product, in which case the submission may be made four years following the original drug approval. That is, under the provisions of the Hatch-Waxman Act, December 19, 2020 was the earliest date that a generic competitor could submit an ANDA to the FDA requesting permission to market a generic version of Rubraca. Since that time, generic entities have been permitted to file an ANDA for rucaparib with a Paragraph IV certification asserting that one or more patents listed in the Orange Book for Rubraca are either not infringed, invalid, or not enforceable. We have not received any Paragraph IV certification notice letters, and to our knowledge, no ANDA filings for rucaparib have been made to date. In March 2021, the FDA issued revised draft product-specific guidance for industry on rucaparib camsylate that replaces the guidance previously issued in February 2018. Because rucaparib camsylate is considered a cytotoxic drug, the published FDA guidance requires any party seeking approval for a generic form of rucaparib to file a Bio-IND and recommends showing bioequivalence in "female patients with a deleterious *BRCA* mutation associated with advanced cancer who have been treated with two or more chemotherapies and are receiving a regimen of rucaparib camsylate." The guidance sets forth additional criteria, including the demonstration of bioequivalence to a 90 percent confidence interval. Demonstrating bioequivalence with

Rubraca would only be an initial step in the ANDA approval process. In a potential ANDA litigation, a generic challenger would also need to successfully challenge or design around Orange Book listed patents, some of which do not expire until 2035. If a Paragraph IV Certification is made, the generic company is required to provide a Paragraph IV Notice Letter advising Clovis of the certification. If that occurs, Clovis will have the opportunity to bring a patent infringement action against the generic company. If such a suit is filed within the 45-day period following receipt of the Paragraph IV Notice Letter, the Hatch-Waxman Act provides for a 30-month stay on FDA's ability to grant final approval of the proposed generic product. The 30-month stay generally runs from the date the Paragraph IV Notice Letter is received. The 30-month stay may be shortened or lengthened, including due to a settlement of a lawsuit, a court order (including a decision by the district court on the merits of the case), or patent expiration.

Two European patents in the rucaparib camsylate salt/polymorph patent family (European Patent 2534153 and its divisional European Patent 3150610) were opposed. In particular, opposition notices against European Patent 2534153 were filed by two parties on June 20, 2017. During an oral hearing that took place on December 4, 2018, the European Patent Office's Opposition Division maintained European Patent 2534153 in amended and narrowed form with claims to certain crystalline forms of rucaparib camsylate, including, but not limited to, rucaparib S-camsylate Form A, the crystalline form in Rubraca. Clovis and one opponent, Hexal AG, appealed the written decision of the European Opposition Division and filed reply appeal briefs in November 2019. An oral hearing in the appeal is scheduled on December 8, 2022.

An opposition against European Patent 3150610 was filed by Generics (UK) Limited on April 30, 2020 on grounds similar to those raised in the opposition notices against European Patent 2534153, which grounds are common in such proceedings. Clovis responded to the opposition notice in European Patent 3150610 by amending the claims to be directed to the use of rucaparib maleate in a method of inhibiting PARP activity or treating cancer. That is, the amended claims do not cover Rubraca. During an oral hearing that took place on November 18, 2021, European Patent 3150610 was revoked and the written decision of the European Patent Office was dated December 15, 2021. Clovis filed a notice of appeal on January 28, 2022 and an appeal brief before April 25, 2022. During the appeal, the effect of the Opposition Division's decision is suspended, and the patent remains in force until a Technical Board of Appeals issues its own decision.

We have filed for patent term extension under a supplementary protection certificate for Rubraca based on European Patent 2534153 and believe that extension could be available to 2033. Additionally, in Europe, regulatory exclusivity is available for ten years, plus one year for a new indication; therefore, we have regulatory exclusivity for Rubraca, including all forms of rucaparib, in Europe until 2028, and if the EMA approves a subsequent indication that brings significant clinical benefit in comparison with existing therapies, until 2029.

We obtained rights to lucitanib by acquiring EOS in November 2013, along with its license agreement with Advenchen. We have rights to develop and commercialize lucitanib on a global basis, excluding China. Composition of matter and method of use patent protection for lucitanib and a group of structurally-related compounds is issued in the United States, Europe, and Japan and is issued or pending in other jurisdictions. In the United States, the composition of matter patent will expire in 2030, and in other jurisdictions, it expires in 2028. We believe that patent term extension could be available to extend our composition of matter patent up to five years beyond the scheduled expiration under the Hatch-Waxman Act in the United States, and similar provisions in other jurisdictions. Additionally, patents directed to methods of manufacturing lucitanib are issued in the United States, Europe and China.

In September 2019, we acquired rights from 3BP to develop and commercialize a peptide-targeted radionuclide therapy ("PTRT") and imaging agent targeting fibroblast activation protein ("FAP"), including FAP-2286. We hold global development rights, and U.S. and global commercialization rights, excluding Europe (inclusive of Russia, Turkey and Israel), where 3BP retains rights. Patent applications are pending that claim FAP-2286 generically and specifically (including with respect to composition of matter) that, if issued, would have expiration dates in 2040.

In addition, we intend to seek patent protection whenever available for any products or product candidates and related technology we acquire in the future.

The patent positions of pharmaceutical firms like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, we do not know whether any of the product candidates we acquire, or license will gain patent protection or, if any patents are issued, whether they will provide significant proprietary protection or will be challenged,

circumvented or invalidated. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, until that time we cannot be certain that we were the first to file any patent application related to our product candidates. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office ("U.S. PTO") to determine priority of invention or in opposition or other third-party proceedings in the U.S. or a foreign patent office, either of which could result in substantial cost to us, even if the eventual outcome is favorable to us. There can be no assurance that the patents, if issued, would be held valid by a court of competent jurisdiction. An adverse outcome in a third-party patent dispute could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using specific compounds or technology.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries or jurisdictions in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. PTO in granting a patent or may be shortened if a patent is terminally disclaimed over another patent.

The patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-U.S. jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products.

To protect our rights to any of our issued patents and proprietary information, we may need to litigate against infringing third parties, or avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights. These types of proceedings are often costly and could be very time-consuming to us, and we cannot assure you that the deciding authorities will rule in our favor. An unfavorable decision could allow third parties to use our technology without being required to pay us licensing fees or may compel us to license needed technologies to a third-party. Such a decision could even result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. To the extent prudent, we intend to bring litigation against third parties that we believe are infringing one or more of our patents.

In addition, we have sought and intend to continue seeking orphan drug status whenever it is available. If a product which has an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, meaning that the applicable regulatory authority may not approve any other applications to market the same drug for the same indication, except in certain very limited circumstances, for a period of seven years in the United States and ten years in Europe. Orphan drug designation does not prevent competitors from developing or marketing different drugs for an indication.

We also rely on trade secret protection for our confidential and proprietary information. No assurance can be given that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. However, we believe that the substantial costs and resources required to develop technological innovations will help us to protect the competitive advantage of our products.

It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual shall be our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for commercial use, or non-clinical studies and clinical trials and intend to do so in the future. We currently have long-term agreements with third-party contract manufacturing organizations ("CMOs") for the production of the active ingredient and final product for Rubraca. We do not own or operate manufacturing facilities for the production of commercial and clinical quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing, we are working with our current third-party suppliers to ensure sufficient capacity to meet our manufacturing requirements. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

We have developed the process for manufacturing Rubraca's active pharmaceutical ingredient ("API") to a degree sufficient to meet clinical demands and projected commercial requirements. Manufacturing of Rubraca API is being performed by Lonza Ltd ("Lonza"). Manufacturing operations for an advanced intermediate, which is the inventory prior to conversion to API, was expanded to a second Lonza site during 2019. The Rubraca drug product formulation and manufacturing process to produce that formulation have been developed to a degree sufficient to meet clinical demands and projected commercial requirements. A single third-party CMO capable of both formulation development and drug product manufacturing is currently producing the Rubraca drug product.

To date, our third-party manufacturers have met our manufacturing requirements and we expect them to meet anticipated full-scale commercial demands.

Lonza Agreement - Rubraca

On October 3, 2016, we entered into a Manufacturing Services Agreement (the "Agreement") with Lonza for the long-term manufacture and supply of the API for rucaparib. Under this agreement, Lonza is a non-exclusive manufacturer of the Rubraca API during the 10-year term of the agreement. Lonza constructed, in an existing Lonza facility, a production train to manufacture of the Rubraca API. The production train provides manufacturing capacity to meet our currently anticipated needs for commercial supply of Rubraca API. We made scheduled capital program fee payments toward capital equipment and other costs associated with the construction of the production train. Beginning in the fourth quarter of 2018, once the facility was operational, we were obligated to pay a fixed facility fee each quarter for the duration of the Agreement, which expires on December 31, 2025, unless extended by mutual consent of the parties.

At the time we entered into the Agreement, we evaluated the Agreement as a whole and bifurcated into lease and non-lease components, which consisted of an operating lease of warehouse space, financial lease of equipment, purchase of leasehold improvements and prepaid manufacturing costs based upon the relative fair values of each of the deliverables. During October 2018, the production train was placed into service and we recorded the various components of the Agreement.

On June 16, 2021, we entered into amendment no. 2 of the Agreement with Lonza ("Amendment 2"). Pursuant to the terms of Amendment 2, we paid Lonza $1.1 million to repurpose the production train so that Lonza will be able to use the facility to manufacture other products for third parties in addition to API for Clovis. Lonza is guaranteeing a minimum percentage usage of this production train for third parties and Lonza would reduce our fixed facility fee starting in 2023 based on this minimum percentage usage. If Lonza is able to utilize greater than the minimum guaranteed percentage, it will increase the reduction to our fixed facility fee.

Either party may terminate the agreement due to a material breach of the agreement by the other party, subject to prior written notice and a cure period. We may terminate the agreement, subject to 90 days' prior written notice, in the event Rubraca is withdrawn from the market for certain reasons. In the event of such a termination by us, or termination by Lonza due to material breach by us, we are obligated to compensate Lonza for any services rendered, or for which costs have been incurred by Lonza in anticipation of services to be provided to us, and to pay to Lonza the remaining amount of any capital program fees and quarterly fixed facility fees for the remainder of the term of the agreement. In the event we terminate the agreement due to material breach by Lonza, Lonza is obligated to repay all or a portion of the capital program fees previously paid by us.

FAP-2286

The precursor (API without radionuclide) for FAP-2286 is currently being produced by a CMO. To date, the current production process has been sufficient to satisfy immediate clinical demands. We may undertake additional development work to further optimize the precursor manufacturing process. The finished drug product for ^{177}Lu -FAP-2286 is currently being manufactured at a CMO. The current product and process are sufficiently developed to meet immediate clinical demands. Additional scale-up work and/or additional production capacity will be necessary to support larger clinical development or commercialization requirements.

In October 2021, we entered into a clinical supply agreement with ITM Isotope Technologies Munich SE that provides us with ITM's therapeutic radioisotope no-carrier-added ^{177}Lu, EndolucinBeta®, for use in the clinical development of FAP-2286 for the next five years.

Lucitanib

The API for lucitanib is currently being produced by a CMO. To date, the current production process has been sufficient to satisfy immediate clinical demands. We may undertake additional development work to further optimize the active pharmaceutical ingredient manufacturing process. The finished drug product for lucitanib is currently being manufactured at a CMO. The current product and process are sufficiently developed to meet immediate clinical demands. Additional scale-up work and/or additional production capacity will be necessary to support larger clinical development or commercialization requirements.

Commercial Operations

Our commercial organizations in the U.S. and Europe are in place and supporting the commercial sale of Rubraca. We believe the oncology market for Rubraca is addressable with a targeted sales and marketing organization, with capabilities that include the management of key accounts such as managed care organizations, group-purchasing organizations, oncology group networks and government accounts. We sell Rubraca through a limited distribution network consisting of select number of specialty pharmacies and distributors. Healthcare providers prescribe Rubraca to patients and the specialty pharmacies and distributors dispense Rubraca directly to patients. We intend to continue promoting Rubraca ourselves for its current indications and any additional indications we may obtain in the future. We retain the rights to Rubraca in the rest of the world.

In October 2020, we adopted a new U.S. commercial strategy to address a challenging sales environment resulting from a trend toward reduced in-person access for oncology commercial teams to oncology practices in general, which has been further accelerated by COVID-19, which has severely limited oncology patient visits and cancer diagnoses. Physicians increasingly prefer digital communications and virtual peer-to-peer interactions which they can access when they choose. The new hybrid strategy elevates digital programming, virtual communication and peer-to-peer interactions while reducing in-person promotion, and the remaining in-person activities will be much more targeted. This hybrid strategy does not require as large a U.S. commercial organization, and in early November 2020 the size of the organization was reduced to approximately 85 employees.

Customers

We are currently approved to sell Rubraca in the U.S. and Europe markets. We distribute our product principally through a limited number of specialty distributor and specialty pharmacy providers, collectively, our customers. Our customers subsequently sell our products to patients and health care providers. We do not believe the loss of one of these customers would significantly impact the ability to distribute our product as we expect that sales volume would be absorbed evenly by the remaining customers. Separately, we have arrangements with certain payors and other third parties that provide for government-mandated and privately-negotiated rebates, chargebacks and discounts.

Employees

As of February 17, 2022, we had 413 employees, of which 278 were employed in the U.S. and 135 were employed outside of the U.S. None of our U.S. employees are represented by labor unions, and a very small number of international employees are covered by collective bargaining agreements.

Our success depends upon our ability to retain and attract highly qualified management and technical personnel. Talent management is critical to our ability to execute on our long-term growth strategy. We appreciate the importance of retention, growth and development of our employees. We continue to be committed to an inclusive culture which values equality, opportunity and respect. In support of our inclusive culture, we believe we offer competitive compensation and benefits, including an annual pay gap assessment; provide respectful workplace training to strengthen employee understanding; and strive to recruit a diverse talent pool across all levels of the organization.

Employee safety and wellbeing is of paramount importance to us in any year and was of particular focus in our fiscal years 2020 and 2021 in light of COVID-19. In response to the pandemic, we provided productivity and collaboration tools and resources for employees working remotely, including training and toolkits to help leaders effectively lead and manage remote teams. In addition, throughout 2021 we continued to enhance and promote programs to support our employees' physical and mental wellbeing.

About Clovis

We were incorporated under the laws of the State of Delaware in April 2009 and completed our initial public offering of our common stock in November 2011. Our common stock is listed on the NASDAQ Global Select Market under the symbol "CLVS." Our principal executive offices are located at 5500 Flatiron Parkway, Suite 100, Boulder, Colorado 80301, and our telephone number is (303) 625-5000. We maintain additional offices in San Francisco, California, Oakland, California, Cambridge, UK, London, UK, Milan, Italy and in several other locations in Europe. Our website address is *www.clovisoncology.com*. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this report.

Available Information

As a public company, we file reports and proxy statements with the Securities and Exchange Commission ("SEC"). These filings include our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and proxy statements on Schedule 14A, as well as any amendments to those reports and proxy statements, and are available free of charge through our website as soon as reasonably practicable after we file them with, or furnish them to, the SEC. Once at *www.clovisoncology.com*, go to Investors & News/SEC Filings to locate copies of such reports. The SEC also maintains a website at www.sec.gov that contains reports, proxy statements and other information regarding us and other issuers that file electronically with the SEC.

ITEM 1A. RISK FACTORS

Our business faces significant risks and uncertainties. Certain factors may have a material adverse effect on our business prospects, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in or incorporated by reference into this Annual Report on Form 10-K and our other public filings with the SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

Risk Factor Summary

Our business operations are subject to numerous risks and uncertainties, including those outside of our control, that could cause our business, financial condition or operating results to be harmed, including risks regarding the following:

- we have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future which, together with our limited working capital and unpredictable Rubraca sales, raises substantial doubt about our financial viability and as to whether we will be able to continue as a going concern;
- we will require substantial additional funding which may not be available to us on acceptable terms, or at all, for a number of reasons, including market conditions, our ability to generate positive data from our clinical studies, and the need for our stockholders to approve an amendment to our certificate of incorporation to increase the number of shares of common stock that we are authorized to issue, and failure to obtain additional funding may impact our ability to continue our development programs and successfully commercialize Rubraca and our ability to continue as a going concern;

- the impact of the COVID-19 pandemic on our revenues and our ability to continue to operate our business;
- servicing our long-term debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt;
- we may not be able to raise the funds necessary to repay our debt upon a fundamental change, and provisions in our debt could delay or prevent an otherwise beneficial takeover of us;
- we are highly dependent on revenues from the sale of Rubraca, and the rate and degree of market acceptance and commercial viability, including the safety, efficacy and potency of Rubraca and our other product candidates may limit the commercial success of Rubraca;
- if our sales, marketing and distribution capabilities for Rubraca or other product candidates for which we obtain marketing approval are inadequate, we may be unable to generate sufficient revenue from sales of our products;
- we cannot give any assurance that the Rubraca development program in other lines of therapies and indications will be successful or that our other product candidates will receive regulatory approval;
- our expectations regarding the FDA and other regulatory authorities' interpretation of our data and information on our product candidates and the impact on our business of the FDA's and other regulatory authorities' interpretation of our submissions, filing decisions by the FDA and other regulatory authorities, potential advisory committee meeting dates and advisory committee recommendations, and FDA and other regulatory authorities product approval decisions and related timelines;
- the success of competing drugs that are or become available;
- the success and timing of our non-clinical studies and clinical trials;
- our ability to verify the clinical benefit of Rubraca through our confirmatory trials and to satisfy other post-marketing requirements and post-marketing commitments, our ability to obtain and maintain regulatory approval of Rubraca and our other product candidates, and the labeling under Rubraca and any other approval we may obtain;
- our ability to engage and retain third-party manufacturers with sufficient capability and capacity to support the commercialization of Rubraca and our other product candidates, and the performance of such third-party manufacturers;
- our ability to obtain and maintain intellectual property protection for our product candidates, including our ability to defend our intellectual property against challenges;
- our ability to maintain our collaborations with our licensing partners to develop our product candidates;
- the size and growth of potential markets for our product candidates and our ability to serve those markets;
- the loss of key scientific or management personnel;
- regulatory developments in the United States and foreign countries;
- our operating results are difficult to predict and may fluctuate, and if our operating results are below the expectations of investors or analysts, the trading price of our stock could decline;
- the price of our stock has been, and may continue to be volatile, which will impact the value of your investment and our ability to raise additional capital on favorable terms, or at all;
- future sales and issuances of our common stock or rights to purchase our common stock, including through our equity incentive plans, could result in dilution of your investment and cause our stock price to fall.

Risks Related to the COVID-19 Pandemic

The outbreak of COVID-19 could materially adversely affect our business.

On January 30, 2020, the World Health Organization (the "WHO") declared that the recent novel coronavirus disease ("COVID-19") outbreak was a public health emergency of international concern, and on March 11, 2020 the WHO declared the COVID-19 outbreak a pandemic. This has resulted in increased travel restrictions, quarantines, "work-at-

home" and "shelter-in-place" orders and extended shutdown of certain non-essential businesses in the United States, and European and Asia-Pacific countries, including countries in which we commercialize Rubraca and countries in which we have planned or active clinical trials. With a renewed rise in the number of cases of the coronavirus in certain parts of the United States and Europe and the ongoing uncertainty regarding future trends in cases, these restrictions, quarantines, shutdowns and other disruption to businesses globally continue to evolve and, in many areas, increase. The effects of the coronavirus are difficult to assess or predict.

Our ability to generate product revenue for the year and quarter ended December 31, 2021 was negatively affected by the COVID-19 pandemic, primarily due to the ongoing effect the pandemic has had on oncology treatment and practice, and in particular, in ovarian cancer, resulting in fewer diagnoses and fewer patients going to in-person office visits in the U.S. As a result of the COVID-19 pandemic, our U.S. and European sales forces have had physical access to hospitals, clinics, doctors and pharmacies curtailed and/or have been limited. Our European launches occurred in an environment in which our field-based personnel were not allowed to visit hospitals beginning as early as late February 2020. Similarly, we launched Rubraca for prostate cancer in the U.S beginning in May 2020, but our physical access to hospital, clinics, doctors and pharmacies remains limited. It is difficult to discern or predict any trend in new patient starts due to the unpredictability of the COVID-19 situation and the changing competitive landscape.

The outbreak of COVID-19 has had a major impact on the financial markets, the global economy or the economies of particular countries or regions. Specifically, the COVID-19 outbreak could result in reduced operations of third-party manufacturers upon whom we rely, disrupt our supply chain, or otherwise limit our ability to obtain sufficient materials to manufacture Rubraca and our product candidates. While we believe that we have sufficient supply of Rubraca and our product candidates to continue our commercial and clinical operations as planned, Rubraca and our product candidates, or materials contained therein, come from facilities located in areas impacted by COVID-19 or that may be impacted, as the COVID-19 outbreak or its disruption worsens. If any third party in our supply or distribution chain for materials or finished product are adversely impacted by restrictions resulting from the COVID-19 outbreak, including staffing shortages, production slowdowns and disruptions in delivery systems, our supply chain may be disrupted, limiting our ability to manufacture and distribute Rubraca for commercial sales and our product candidates for our clinical trials and research and development operations. There is no guarantee that the recent COVID-19, or any potential future, outbreak would not impact our future supply chain, which could have a material adverse impact on our clinical trial plans and business operations.

Our sales force has had physical access to hospitals, clinics, doctors and pharmacies curtailed and/or has been limited, which may have a material adverse effect on our future sales. While digital tools are available to our field employees to facilitate remote meetings with healthcare providers, we cannot ensure that these methods will be effective. Additionally, patients who might be currently using Rubraca, or might otherwise be eligible to use our products, may be unable to meet with their healthcare providers in-person, which may reduce the number of prescription refills or new patient starts, affecting our revenues from Rubraca both in our currently approved ovarian cancer indications, as well as impacting our current launch in *BRCA*-mutant metastatic castration-resistant prostate cancer, which was approved during the second quarter of 2020.

We did not see material disruption to our clinical trials as a result of the COVID-19 pandemic for the three and twelve months ended December 31, 2021. However, with the increase in cases of COVID-19 due to the Omicron variant, and the potential for quarantines, unavailability of medical services regarded as non-essential, or reluctance of patients to seek treatment, we may see delays in enrollment during 2022. For example, new patient recruitment in clinical studies, including LuMIERE, may be affected and the conduct of clinical trials may vary by geography as some regions are more adversely affected.

In addition, COVID-19 could affect our employees, our agents and their employees or the employees of companies with which we do business, thereby disrupting our business operations. We have implemented work-at-home policies and may experience limitations in employee resources. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. The effects of working from home and other burdens imposed by COVID-19 on individuals may impact our employee retention. In addition, our reliance on personnel working from home could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, manufacturing sites, research or clinical trial sites and other important agencies and contractors.

On March 18, 2020, the Families First Coronavirus Response Act ("FFCR Act"), and on March 27, 2020, the Coronavirus Aid, Relief and Economic Security ("CARES") Act were each enacted in response to the COVID-19 pandemic. The FFCR Act and the CARES Act contain numerous income tax provisions, such as relaxing limitations on the deductibility of interest and the use of net operating losses arising in taxable years beginning after December 31, 2017. On March 11, 2021, President Biden signed an additional coronavirus relief package entitled the American Rescue Plan Act of 2021 ("ARPA"), which included, among other things, provisions relating to stimulus payments to some Americans, extension of several CARES Act relief programs, expansion of the child tax credit, funding for vaccinations and other COVID-19 related assistance programs. The CARES Act, FFCR Act, and the ARPA have not had a material impact on the Company; however, we will continue to examine the impacts that these Acts, as well as any future economic relief legislation, may have on our business.

The trading prices for our common stock and of other biopharmaceutical companies have been highly volatile as a result of the coronavirus pandemic. As a result of this volatility and uncertainties regarding the future impact of COVID-19 on our business and operations, we may face difficulties raising capital or may only be able to raise capital on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the coronavirus could materially and adversely affect our business and the value of our common stock. A number of governments in places where we have operations have adopted stimulus programs to assist businesses effected by COVID-19, including by facilitating lending arrangements. We may access these loan programs for additional working capital although there can be no guarantee that we will obtain any such loans and we do not currently know the terms of such loan programs.

The effectiveness of external parties, including governmental and non-governmental organizations, in combating the spread and severity of COVID-19 could have a material impact on the losses we experience. These events could cause a material adverse effect on our results of operations in any period and, depending on their severity, could also materially and adversely affect our financial condition.

Risks Related to Our Financial Position and Capital Requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future, which together with our limited working capital raises substantial doubt about our financial viability and as to whether we will be able to continue as a going concern.

Our auditor's report on our financial statements for the year ended December 31, 2021, includes an explanatory paragraph related to the existence of substantial doubt about our ability to continue as a going concern. We are a biopharmaceutical company with a limited operating history. We are not profitable and have incurred losses in each year since our inception in April 2009. For the years ended December 31, 2021, 2020 and 2019, we had net losses of $264.5 million, $369.2 million and $400.4 million, respectively. As of December 31, 2021, we had an accumulated deficit of $2,877.3 million. Biopharmaceutical product development is a highly speculative undertaking and involves a high degree of risk and requires substantial capital investment. We continue to incur significant research and development and other expenses related to our ongoing operations. We have limited working capital. We have received regulatory approval to market Rubraca in the U.S. and in Europe, but do not know whether Rubraca will be approved in other jurisdictions or in additional tumor types and indications, or whether it will achieve market acceptance and be commercially successful in the long run. Although we generate revenues from product sales, these revenues have not been sufficient, and may never be sufficient, to support our operations. Rubraca revenues have not been consistent in prior quarters, mainly as a result of the impact of COVID-19 and competition from other products on the market. We expect to continue to incur losses and negative cash flows for the foreseeable future. We require significant cash resources to execute our business plans and we will need to raise additional cash to continue to fund our operating plan. We expect to finance our operating plan through a combination of public or private equity or debt offerings, collaborations, strategic alliances and other similar licensing arrangements in both the short term and the long term. We cannot be certain that additional funding will be available on acceptable terms, or at all, for a number of reasons, including market conditions, our ability to generate positive data from our clinical studies, and the need for our stockholders to approve an amendment to our certificate of incorporation to increase the number of shares of common stock that we are authorized to issue. The aforementioned factors, which are largely outside of our control, raise substantial doubt about our ability to continue as a going concern within one year from the date of filing of this annual report. The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of asset amounts or the classification of

liabilities that might be necessary should we be unable to continue as a going concern within one year after the date of filing of this annual report. If we are forced to scale down, restructure, limit or cease operations, our stockholders could lose all of their investment in our Company.

We will require substantial additional funding which may not be available to us on acceptable terms, or at all. If we fail to obtain additional financing, we will be unable to continue our development programs, fund our operating plan and continue as a going concern.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to advance the clinical development of our products and launch and commercialize our products. Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we do not expect in the foreseeable future and which we may never do in sufficient amounts, we expect to finance our operating plan through a combination of public or private equity or debt offerings, collaborations, strategic alliances and other similar licensing arrangements in both the short term and long term. We cannot be certain that additional funding will be available on acceptable terms, or at all. Our ability to obtain additional financing will depend on a number of factors, including, among others, our ability to generate positive data from our clinical and pre-clinical studies, the condition of the capital markets and the other risks described in these risk factors. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will not be able to fund our operating plan and may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our products. Any of these events could significantly harm our business, financial condition and prospects. We may not be able to continue our operations.

In addition, in order to continue to raise capital through the sale of equity securities (or securities convertible into our equity securities), we will need our stockholders, at the 2022 Annual Meeting of Stockholders, to consider again and to approve a proposal to amend our certificate of incorporation to increase the number of shares of common stock that we are authorized to issue. We cannot be certain that our stockholders will approve such a proposal. In the event our stockholders do not approve such a proposal, our ability to raise capital to fund our operations beyond the next 12 months will be significantly limited and we will need to consider potentially more costly sources of funding, potentially through incurring further indebtedness or entering into strategic partnerships or licensing arrangements for one or more of our products or product candidates in which we may have to give up certain of our future commercialization rights for interim funding. We cannot be certain that such other sources of funding will be available to us or on acceptable terms or in sufficient amounts to meet our requirements and to continue our operations.

Servicing our long-term debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.

As of December 31, 2021, we had $300.0 million outstanding aggregate principal amount of 1.25% convertible senior notes due 2025 (the "2025 Notes"), $85.8 million outstanding aggregate principal amount of 4.50% convertible senior notes due 2024 (the "2024 Notes (2019 Issuance)"), and $57.5 million outstanding aggregate principal amount of a new series of 4.50% Convertible Senior Notes due 2024 (the "2024 Notes (2020 Issuance))" and together with the 2024 Notes and 2025 Notes, the "Notes"). In addition, as of December 31, 2021, we had $147.2 million outstanding aggregate principal amount pursuant to our ATHENA clinical trial financing agreement. We are obligated to begin repaying the ATHENA clinical trial financing on a quarterly basis, beginning on the earliest to occur of (i) the termination of the ATHENA Trial, (ii) the approval by the FDA of an update to the label portion of the Rubraca new drug application ("NDA") to include in such label the treatment of an indication resulting from the ATHENA Trial, (iii) the date on which we determine that the results of the ATHENA Trial are insufficient to achieve such an expansion of the Rubraca label to cover an indication based on the ATHENA Trial and (iv) September 30, 2022 (the "Repayment Start Date").

Our ability to make scheduled payments of interest and principal on the Notes, to pay the repurchase price for the Notes on a fundamental change or to begin repaying the ATHENA clinical trial financing when due, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. We may not have sufficient cash in the future to service our debt. If we are unable to generate such cash flow or secure additional sources of funding, we may be required to adopt one or more alternatives, such as restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these

activities or engage in these activities on desirable terms. If we fail to meet our obligations under the Notes, we will be in default, which may also cause a default under, and an acceleration of, our other debt obligations.

We may not be able to raise the funds necessary to repurchase the Notes upon a fundamental change, or the ATHENA clinical trial financing agreement upon a change of control, and our future and current debt may contain limitations on our ability to repurchase the Notes.

If we undergo a fundamental change, as defined in the indenture, prior to the maturity date of the Notes, holders may require us to repurchase for cash all or any portion of the Notes at a fundamental change repurchase price equal to 100% of the principal amount of the Notes to be repurchased plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, in the event of a change of control of us, we must pay to the lenders under the ATHENA clinical trial financing agreement, 1.75 times the amount we have borrowed thereunder if the change of control occurs prior to the Repayment Start Date, or 2 times the amount we have borrowed thereunder if the change of control occurs after the Repayment Start Date (minus the amount of all quarterly payments previously paid to the lenders) (the "Discharge Amount"). We may not have or be able to borrow the funds required to repurchase the Notes on the fundamental change repurchase date. In addition, our ability to repurchase the Notes may otherwise be limited by law, regulatory authority or agreements governing our future indebtedness, including limitations on repurchase of certain debt set forth in the ATHENA clinical trial financing agreement. Our failure to repurchase the Notes at a time when the repurchase is required by the indenture would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing other current indebtedness, such as the ATHENA clinical trial financing agreement, or our future indebtedness. For example, an event of default under the ATHENA clinical trial financing agreement (which includes, among other events, breaches or defaults under or terminations of our material in-license agreements related to Rubraca and defaults under our other material indebtedness), the lenders have the right to declare the Discharge Amount to be immediately due and payable. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the Notes when required.

We may incur substantially more debt or take other actions which would intensify the risks discussed above; and we may not generate cash flow from operations in the future sufficient to satisfy our obligations under the Notes, the ATHENA clinical trial financing agreement and any future indebtedness we may incur.

We may incur substantial additional debt in the future, subject to the restrictions contained in any debt instruments that we enter into in the future, some of which may be secured debt, such as the ATHENA clinical trial financing agreement. We are not restricted under the terms of the indenture governing the Notes from incurring additional debt, securing existing or future debt, recapitalizing our debt or taking a number of other actions that are not limited by the terms of the indenture governing the Notes that could have the effect of diminishing our ability to make payments on the Notes or the ATHENA clinical trial financing agreement when due. Our ability to refinance the Notes or future indebtedness will depend on the capital markets and our financial condition at such time. In addition, agreements that govern any future indebtedness that we may incur may contain financial and other restrictive covenants that will limit our ability to engage in activities that may be in our long-term best interests. Our failure to comply with those covenants could result in an event of default that, if not cured or waived, could result in the acceleration of some or all of our debt.

Provisions in the indenture and the ATHENA clinical trial financing agreement could delay or prevent an otherwise beneficial takeover of us.

Certain provisions in the Notes and the indentures governing the Notes, and in the ATHENA clinical trial financing agreement, could make a third-party attempt to acquire us more difficult or expensive. For example, if a takeover constitutes a fundamental change, then holders will have the right to require us to repurchase their notes for cash. In addition, if a takeover constitutes a make-whole fundamental change, then we may be required to temporarily increase the conversion rate. In either case, and in other cases, our obligations under the Notes, the indentures governing the Notes and the ATHENA clinical trial financing agreement could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management, including in a transaction that holders or holders of our common stock may view as favorable.

Risks Related to Our Business and Industry

We are highly dependent on the commercial success of Rubraca; Rubraca may not achieve market acceptance and may not be commercially successful and we may not attain profitability and positive cash flow from operations.

Rubraca is commercially available in the U.S. and Europe. The degree of market acceptance and the commercial success of Rubraca will depend on a number of factors, including:

- the effectiveness of our sales and marketing strategy and operations;
- maintaining compliance with all regulatory requirements applicable to Rubraca and our commercial activities, including the post-marketing requirements and post-marketing commitments required by the FDA and the EMA, to verify Rubraca's clinical benefit or safety by completing certain confirmatory trials, pharmacology studies and additional diagnostic development;
- the acceptance of Rubraca by patients and the medical community and the availability, perceived advantages and relative cost, safety and efficacy of alternative and competing products and therapies;
- the continued acceptable safety profile of Rubraca and the occurrence of any unexpected side effects, adverse reactions or misuse, or any unfavorable publicity in these areas;
- the ability of our third-party manufacturers to manufacture commercial supplies of Rubraca, to remain in good standing with regulatory agencies, and to develop, validate and maintain commercially viable manufacturing processes that are, to the extent required, compliant with cGMP regulations;
- the availability of coverage and adequate reimbursement from managed care plans, private health insurers and other third-party payors and the willingness and ability of patients to pay for Rubraca;
- the development or commercialization of competing products or therapies;
- marketing and distribution support for Rubraca, including the degree to which the approved labeling supports promotional initiatives for commercial success;
- the actual market size for Rubraca, which may be different than expected;
- our ability to enforce our intellectual property rights in and to Rubraca;
- our ability to avoid third party patent interference or patent infringement claims; and
- our ability to obtain regulatory approvals, including for pricing and reimbursement, to commercialize Rubraca in markets outside of the U.S. and Europe.

As many of these factors are beyond our control, we cannot assure you that we will be able to continue to grow meaningful revenue through the sale of Rubraca. In addition, we may experience significant fluctuations in sales of Rubraca from period to period. We have two other product candidates, lucitanib and FAP-2286, in clinical development. Any inability on our part to successfully commercialize Rubraca in the United States, Europe and any other territories where it may be approved, or any significant delay in such approvals, could have a material adverse impact on our ability to execute upon our business strategy and, ultimately, to generate sufficient revenues from Rubraca to reach or maintain profitability or sustain our anticipated levels of operations.

If our sales, marketing and distribution capabilities for Rubraca or our product candidates for which we obtain marketing approval are inadequate, we may be unable to generate revenue from sales of our products.

Prior to the launch of Rubraca, we had not commercialized any drug products as a company. To achieve commercial success for Rubraca and any product candidate that may be approved by the FDA or comparable foreign regulatory authorities, we must continue to maintain or expand our sales, marketing, managerial and other nontechnical capabilities or make arrangements with third parties to perform these services. We are competing with companies that currently have extensive, well-funded, and more experienced sales and marketing operations. We may be unable to compete successfully against these more established companies.

We have built a field organization and other capabilities for the sales, marketing and distribution of Rubraca in the United States and in Europe, and there are significant risks involved with building and managing a sales organization. Factors that may inhibit our efforts to effectively commercialize Rubraca on our own include:

- our inability to recruit, train, retain and incentivize adequate numbers of qualified and effective sales and marketing personnel;
- the inability of sales personnel to generate sufficient sales leads and to obtain access to physicians or persuade adequate numbers of physicians to use or prescribe Rubraca; and
- our inability to effectively manage a geographically dispersed sales and marketing team.

If we are unable to maintain effective sales, marketing and distribution capabilities for Rubraca or if we are unable to fully establish and maintain sales, marketing and distribution capabilities for Rubraca outside of the United States or for any other product candidate for which we obtain marketing approval, whether independently or with third parties, we may not be able to generate product revenue or may not become profitable. If the cost of establishing and maintaining a sales and marketing organization exceeds the cost-effectiveness of doing so, we may not become profitable.

With respect to our product candidates, we may elect to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems in certain territories. To the extent that we enter into licensing or co-promotion arrangements for any of our product candidates, our product revenue may be lower than if we directly marketed or sold our approved products. In addition, any revenue we receive as a result of such arrangements would depend in whole or in part upon the efforts of such third parties, which may not be successful and are generally not within our control. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates that receive regulatory approval. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

We cannot give any assurance that the Rubraca development program in other lines of therapies and indications will be successful or that our other product candidates will receive regulatory approval.

To date, we have invested a significant portion of our efforts and financial resources in the acquisition and development of our product candidates. Our business depends entirely on the successful development and commercialization of our product candidates.

Each of our product candidates requires clinical development, management of clinical, non-clinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, building of a commercial organization and significant marketing efforts in order to generate any revenues from product sales. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities. To date, we have received regulatory approval from the FDA and EMA to market Rubraca in the United States and Europe, respectively. We may not receive regulatory approvals for Rubraca for broader indications and lines of therapy or other tumor types and we may never receive regulatory approval for other product candidates. In addition, certain of our product development plans may contemplate the development of companion diagnostics by third-party collaborators. Companion diagnostics are subject to regulation as medical devices and must themselves be approved for marketing by the FDA or certain other foreign regulatory agencies before our product candidates may be commercialized.

We cannot be certain that Rubraca will be successfully developed to expand its current label to include other indications or that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. Two of our product candidates, CO-101 and rociletinib, encountered development and regulatory setbacks after initial promising data, leading us to discontinue enrollment in ongoing clinical trials. Even if we successfully obtain regulatory approvals to market one or more of our other product candidates, our revenues will be dependent, in part, upon our diagnostic collaborators' ability to obtain regulatory approval of the companion diagnostics, where required, to be used with our product candidates, as well as the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates, and for other indications for Rubraca, in the United States, Europe and in additional foreign countries. While the scope of regulatory approval is similar in other countries, obtaining separate regulatory approval in many other countries requires compliance with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of non-clinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through non-clinical studies and initial clinical trials. It is not uncommon for companies in the biopharmaceutical industry to suffer significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Indeed, based on the negative results of a pivotal study, we ceased further development of our previous product candidate CO-101, and we decided to discontinue ongoing development of rociletinib as a result of the issuance of a Complete Response Letter by the FDA. Additionally, our future clinical trial results may not be successful.

Although we have clinical trials ongoing, we may experience delays in our ongoing clinical trials, and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board ("IRB") approval at each site;
- recruiting suitable patients to participate in a trial;
- developing and validating companion diagnostics on a timely basis;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations, trial sites or manufacturing sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial

prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

The regulatory approval processes of the FDA, EMA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for Rubraca in other indications and lines of therapy or for our other product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have obtained regulatory approval for Rubraca in the United States and Europe, and it is possible that Rubraca may not obtain regulatory approval for broader indications and lines of therapy or other tumor types or that any of our other existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Indeed, with the issuance of a Complete Response Letter by the FDA with respect to the rociletinib NDA, we decided to discontinue ongoing development of rociletinib.

Our product candidates could fail to receive regulatory approval or approval may be delayed for many reasons, including the following:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or comparable foreign regulatory authorities for approval;
- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from non-clinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, MAA or other submission or to obtain regulatory approval in the United States, the EU or elsewhere;
- the FDA, EMA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA, EMA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing with partners; and
- the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

Even if we receive regulatory approval for our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if and when approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and clinical trials and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA, EMA or comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, pricing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practices and good clinical practices for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA, EMA and comparable foreign authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

All of the foregoing limitations, obligations, and requirements also apply to Rubraca, for which we have received regulatory approval in the United States and the EU for certain indications.

We may seek approval from U.S. and foreign regulatory authorities for one or more product candidates on a conditional basis with full approval conditioned upon fulfilling the requirements of regulators. For example, we received accelerated approval from the FDA for the initial indication for Rubraca and conditional marketing authorization from the EMA for the initial indication for Rubraca. Each of these approval pathways has certain conditions to approval, some of which may be post-approval, such as the conduct of a post-approval, or confirmatory, trial using due diligence. If we are unable to fulfill the requirements of regulators that are conditions of a product's accelerated or conditional approval, if the confirmatory trial shows unfavorable results or increased or additional undesirable side effects, or if regulators re-evaluate the data or risk-benefit profile of our product candidate, the availability of accelerated or conditional approval may be withdrawn or our conditional approval may not result in full approval or may be revoked or not renewed. Alternatively, we may be required to change a product candidate's labeled indications or even withdraw the product, if approved, from the market.

The FDA's, EMA's and comparable foreign authorities' policies may change, and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States, the EU or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability, which would adversely affect our business. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Rubraca and our other product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if any.

Adverse events ("AEs") attributable to our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or other comparable foreign authorities. Clinical studies conducted to date have generated AEs related to our product candidates, some of which have been serious. Patients treated with Rubraca have commonly experienced nausea, vomiting, constipation, dysgeusia, anemia/decreased hemoglobin, decreased appetite, diarrhea, abdominal pain, thrombocytopenia and fatigue/asthenia. In studies of lucitanib, hypertension, proteinuria and subclinical hypothyroidism requiring supplementation are the most common AEs observed. As is the case with all oncology drugs, it is possible that there may be other potentially harmful characteristics associated with their use in future trials, including larger and lengthier Phase III clinical trials. As we evaluate the use of our product candidates in combination with other active agents, we may encounter safety issues as a result of the combined safety profiles of each agent, which could pose a substantial challenge to that development strategy.

Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA, EMA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related AEs could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- sales of such product may decline;
- regulatory authorities may withdraw or restrict approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- additional nonclinical or clinical studies, changes in labeling or changes to manufacturing processes, specifications and/or facilities may be required
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of the above occurrences would harm or prevent sales of such product, prevent us from achieving or maintain market acceptance of a product candidate, increase our expenses and impair our ability to successfully commercialize Rubraca. As Rubraca is commercially available, it may be used in a wider population and in a less rigorously controlled environment than in clinical studies. As a result, regulatory authorities, healthcare practitioners, third-party payors or patients may perceive or conclude that the use of Rubraca is associated with previously unknown serious adverse effects, undermining our commercialization efforts.

Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics could harm our drug development strategy.

Where appropriate in the context of our clinical development strategy, we seek to identify patient subsets within a disease category who may derive selective and meaningful benefit from the product candidates we are developing. In collaboration with partners, we may develop companion diagnostics to help us to more accurately identify patients within a particular subset, both during our clinical trials and in connection with the commercialization of our product candidates. Companion diagnostics are subject to regulation by the FDA, EMA and comparable foreign regulatory authorities as medical devices and require separate regulatory approval prior to commercialization. We do not develop companion diagnostics internally and thus we are dependent on the sustained cooperation and effort of our third-party collaborators in developing and obtaining approval for these companion diagnostics. We and our collaborators may

encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, our collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales of our products. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain access to an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

We rely on third parties to conduct our non-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing non-clinical and clinical programs. We rely on these parties for execution of our non-clinical and clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP, which are regulations and guidelines enforced by the FDA, the EMA and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going clinical and non-clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially influence our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse effect on our business, financial condition and prospects.

We rely completely on third parties to manufacture our clinical drug supplies and our commercial supplies of Rubraca, and our development and commercialization of any of our product candidates could be stopped, delayed or made less profitable if those third parties fail to maintain approval of the FDA, EMA or comparable foreign regulatory authorities, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. We do not control the manufacturing operations of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP regulatory requirements for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA, EMA or comparable foreign regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have limited control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our products. There are a limited number of suppliers of raw materials that we use to manufacture our drugs, including Chinese suppliers, and there may be a need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our products for clinical trials and for commercial sale. We do not have direct control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any direct agreements for the commercial production of these raw materials. Any significant delay in the supply of a product or product candidate, or the raw material components thereof, due to the need to replace a third-party manufacturer, could considerably delay completion of our clinical trials and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

We are dependent on our third-party manufacturers to conduct process development and scale-up work necessary to support greater clinical development and commercialization requirements for our product candidates. Carrying out these activities in a timely manner, and on commercially reasonable terms, is critical to the successful development and commercialization of our product candidates. We expect that our third-party manufacturers are capable of providing sufficient quantities of our product candidates to meet anticipated clinical and full-scale commercial demands, however if third parties with whom we currently work are unable to meet our supply requirements, we will need to secure alternate suppliers. While we believe that there are other contract manufacturers having the technical capabilities to manufacture our product candidates, we cannot be certain that identifying and establishing relationships with such sources would not result in significant delay or material additional costs. It may also take a significant period of time to establish an alternative source of supply for our products, product candidates and components and to have any such new source approved by the FDA or any applicable foreign regulatory authorities.

We expect to continue to depend on third-party contract manufacturers for the foreseeable future. While we have long-term agreements with Lonza for the manufacture of API for Rubraca and with the manufacturer of the finished drug product, those are our single sources for the supply of Rubraca API and finished drug product, respectively, and we have not entered into agreements with any alternate suppliers. We currently obtain our supplies of finished drug product through individual purchase orders as described in the current supply agreement.

We are subject to risks associated with the availability of key raw materials, such as the radioisotopes used in the manufacture of our product candidates.

The manufacture of our product candidate ^{177}Lu-FAP-2286 and companion imaging agent ^{68}Ga-FAP-2286 will require the use of raw materials that are subject, at times, to global supply constraints that have the potential to delay our work on the products incorporating those raw materials. For example, any limitation on our ability to source adequate supply of lutetium-177 for ^{177}Lu-FAP-2286 could prevent us from gathering sufficient data in clinical trials, or to the extent that we obtain regulatory approval for marketing for this product candidate, a limited supply may prevent us from

meeting commercial demands. Supply constraints for lutetium-177 could also materially increase the manufacturing costs of ^{177}Lu-FAP-2286, which would increase the cost of our clinical trials and reduce the commercial potential of the product candidate.

In addition, we plan to use ^{68}Ga in our development of imaging agent ^{68}Ga-FAP-2286. Increased future demand for ^{68}Ga may exceed current production capacities. If we are not able to obtain sufficient quantities of gallium-68 for use in ^{68}Ga-FAP-2286, we may not be able to gather sufficient data on ^{68}Ga-FAP-2286 to use in clinical trials or to possibly seek the approval of ^{68}Ga-FAP-2286. In addition, to the extent the approval of our product candidates depends on the screening and monitoring of the patient population with a companion imaging agent such as ^{68}Ga-FAP-2286 in our clinical trials, we would experience a corresponding delay in approval and commercialization of these product candidates if we are not able to obtain sufficient ^{68}Ga.

Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, healthcare payors and major operators of cancer clinics.

Even if we obtain regulatory approval for our other product candidates, the product may not gain market acceptance among physicians, health care payors, patients and the medical community, which are critical to commercial success. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the timing of market introduction of such product candidate as well as competitive products;
- the clinical indications for which the drug is approved, and the product label approved by regulatory authorities, including any warnings that may be required on the label;
- the approval, availability, market acceptance and reimbursement for the companion diagnostic;
- acceptance by physicians, major operators of cancer clinics and patients of the drug as a safe and effective treatment;
- the potential and perceived advantages of such product candidate over alternative treatments, especially with respect to patient subsets that we are targeting with such product candidate;
- the safety of such product candidate seen in a broader patient group, including its use outside the approved indications;
- the cost, safety and efficacy of the product in relation to alternative treatments;
- the availability of adequate reimbursement and pricing by third-party payors and government authorities;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects; and
- the effectiveness of our sales and marketing efforts.

If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, healthcare payors and patients, we will not be able to generate significant revenues, and we may not become or remain profitable.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. In addition, the competition in the oncology market is intense. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions (see Part I, Item 1-Business, Competition section).

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. GlaxoSmithKline plc gained rights to Zejula through its acquisition of Tesaro Inc., which was completed in January 2019. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in

our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, drug products that are more effective or less costly than any drug candidate that we are currently developing or that we may develop. If approved, our product candidates will face competition from commercially available drugs, as well as drugs that are in the development pipelines of our competitors and later enter the market.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA, European Commission or other regulatory approval or discovering, developing and commercializing medicines before we do, which would have a material adverse effect on our business.

Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our products profitably.

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs. We have received marketing authorization for Rubraca in the United States and the EU for multiple indications. We intend to seek additional approvals to market Rubraca and other product candidates in the United States, Europe and other selected foreign jurisdictions. Market acceptance and sales of our products in both domestic and international markets will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for any of our products and may be affected by existing and future healthcare reform measures. Government and other third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new drugs and, as a result, they may not cover or provide adequate payment for our products. These payors may conclude that our products are less safe, less effective or less cost-effective than existing or later introduced products, and third-party payors may not approve our products for coverage and reimbursement or may cease providing coverage and reimbursement for these products.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our products. Even if we obtain coverage for our products, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In both the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be a number of legislative and regulatory changes to the health care system that could affect our ability to sell our products profitably. The U.S. government and other governments have shown significant interest in pursuing healthcare reform. In particular, the Medicare Modernization Act of 2003 revised the payment methodology for many products under the Medicare program in the United States. This has resulted in lower rates of reimbursement. In 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "Affordable Care Act"), was enacted. The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers. Such government-adopted reform measures may adversely affect the pricing of healthcare products and services in the United States or internationally and the amount of reimbursement available from governmental agencies or other third-party payors.

Moreover, payment methodologies, including payment for companion diagnostics, may be subject to changes in healthcare legislation and regulatory initiatives. For example, the CMS has begun bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting and, in 2018, the CMS began paying for clinical laboratory services based on a weighted average of reported prices that private payors, Medicare Advantage plans, and Medicaid Managed Care plans pay for laboratory services.

There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Recently there has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, as well as our ability to set satisfactory prices for our products, to generate revenues, and to achieve and maintain profitability.

In some foreign countries, particularly in Europe, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct additional clinical trials that compare the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our product candidates is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability of our products in such country.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Further, we will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

Our industry has experienced a high rate of turnover of management personnel in recent years. Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, especially Patrick J. Mahaffy, our President and Chief Executive Officer, Dr. Lindsey Rolfe, our Executive Vice President of Clinical Development and Pharmacovigilance and Chief Medical Officer, Gillian C. Ivers-Read, our Executive Vice President, Technical Operations and Chief Regulatory Officer and Dr. Thomas Harding, our Executive Vice President and Chief Scientific Officer whose services are critical to the successful implementation of our product candidate acquisition, development and regulatory strategies.

Despite our efforts to retain valuable employees, members of our management, scientific, development and commercial teams may terminate their employment with us on short notice. Pursuant to their employment arrangements, each of our executive officers may voluntarily terminate their employment at any time by providing as little as thirty days advance notice. Our employment arrangements with all of our employees provide for at-will employment, which means that any of our employees could leave our employment at any time, with or, other than our executive officers, without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

As of February 17, 2022, we employed 413 employees. As our development plans and strategies develop, we expect to expand our employee base for managerial, operational, financial and other resources. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we have to offer. In order to induce valuable employees to continue their employment with us, we have provided stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

Our employees and independent contractors, including principal investigators, CROs, consultants and vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants and vendors, may engage in misconduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent failures to comply with the laws and regulations of the FDA and other similar regulatory agencies, provide accurate information to such authorities, comply with manufacturing standards we have established, including cGMP requirements, comply with federal and state data privacy, securities, fraud and abuse and other healthcare laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee or contractor misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Ethics and other compliance policies, but it is not always possible to identify and deter misconduct by employees and contractors, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant effect on our business and results of operations, including the imposition of significant fines or other sanctions.

Our relationships with healthcare professionals, investigators, consultants, customers (actual and potential) and third-party payors are and will continue to be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, transparency and disclosure (or "sunshine") laws, government price reporting, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may affect, among other things, our current activities with clinical study investigators and research subjects, as well as proposed and future sales, marketing, disease awareness, and patient assistance programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, including any kickback, bribe, or certain rebate, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment will be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or special intent to violate the law in order to have committed a violation; in addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;

- federal false claims laws, including the False Claims Act, which impose criminal and civil penalties, including through civil "qui tam" or "whistleblower" actions, against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from federal programs, such as Medicare and Medicaid, that are false or fraudulent, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
- the Health Insurance Portability and Accountability Act of 1996, or HIPAA which imposes criminal and civil liability for, among other things, willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which also imposes certain requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses, as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal civil monetary penalties statute, which prohibits, among other things, the offering or giving of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's election of a particular supplier of items or services reimbursable by a Federal or state governmental program;
- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare and Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal government price reporting laws, which require drug manufacturers to calculate and report complex pricing metrics to government agencies, including CMS, where such reported prices may be used in the calculation of reimbursement and/or discounts on marketed products. Participation in these programs and compliance with the applicable requirements may result in potentially significant discounts on products subject to reimbursement under federal healthcare programs and increased infrastructure costs, and may potentially limit a drug manufacturer's ability to offer certain marketplace discounts; and
- analogous state laws and regulations, such as state anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

In addition, the research and development of our product candidates outside the United States, and any sales of our products or product candidates once commercialized outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs, including investments in infrastructure and additional resources. Because of the breadth of these laws and the

narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities, including our consulting agreements and other relationships with physicians, could be subject to challenge under one or more of such laws. Governmental and enforcement authorities may conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to, without limitation, civil, criminal, and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Compliance with data privacy laws and regulations is complex and could expose us to a variety of risks.

We operate in an environment that relies on the collection, processing, analysis and interpretation of large sets of individuals' personal information, and that also, in many situations, requires that data to be transferred across borders of numerous countries in which there are different, and potentially conflicting, data privacy laws in effect. For example, the EU General Data Protection Regulation ("GDPR"), which took effect in May 2018, and the California Consumer Privacy Act, which took effect in January 2020, impose stringent requirements on how we and third parties with whom we contract collect, share, export or otherwise process personal information, and provide for significant penalties for noncompliance. Breaches of our systems or those of our third-party contractors, or other failures to protect the data we collect from misuse or breach by third parties, could expose such personal information to unauthorized persons.

Any event involving the substantial loss of personal information or other privacy violations could give rise to significant liability, reputational harm, damaged relationships with business partners, and potentially substantial monetary penalties under laws enacted or being enacted around the world. Such events could also lead to restrictions on our ability to use personal information and/or transfer personal information across country borders.

Our business activities may be subject to the Foreign Corrupt Practices Act ("FCPA") and similar anti-bribery and anti-corruption laws.

We are subject to a number of anti-corruption laws, including the U.S. FCPA and the U.K. Bribery Act. Our failure to comply with anti-corruption laws applicable to us could result in penalties, which could harm our reputation and harm our business, financial condition, results of operations, cash flows or prospects. The FCPA generally prohibits companies and their intermediaries from making improper payments to foreign officials for the purpose of obtaining or keeping business and/or other benefits. The FCPA also requires public companies to maintain accurate books and records and devise a system of sufficient internal accounting controls. We regularly review and update our policies and procedures and internal controls designed to provide reasonable assurance that we, our employees, distributors and other intermediaries comply with the anti-corruption laws to which we are subject. However, there are inherent limitations to the effectiveness of any policies, procedures and internal controls, including the possibility of human error and the circumvention or overriding of the policies, procedures and internal controls. There can be no assurance that such policies or procedures or internal controls will work effectively at all times or protect us against liability under these or other laws for actions taken by our employees, distributors and other intermediaries with respect to our business.

The SEC and the Department of Justice continue to view FCPA enforcement activities as a high priority. There is no certainty that all of our employees, agents, contractors or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs and prohibitions on the conduct of our business. Any such violations could materially damage our reputation, our brand, our international operations, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such

product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, if approved. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- increase in insurance premiums;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenues from product sales;
- the inability to commercialize our product candidates; and
- a decline in our stock price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We have a program of product liability insurance covering our ongoing clinical trials; however, the amount of insurance we maintain may not be adequate to cover all liabilities that we may incur. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our internal computer systems, or those used by our CROs or other vendors, contractors or consultants, may fail or suffer security breaches.

We and our business partners maintain sensitive company data on our computer networks, including our intellectual property and proprietary business information, as well as certain clinical trial information. Cybersecurity attacks are becoming more commonplace and include, but are not limited to, malicious software, attempts to gain unauthorized access to data, including by means of ransomware, social engineering or other means, and other electronic security breaches that could lead to disruptions in systems, misappropriation of information and corruption of data. Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. This includes events where we or our CROs, vendors, contractors or consultants are not targeted but are indirectly impacted by a cyber-attack. In addition, in response to the COVID-19 pandemic, a majority of our workforce is currently working remotely. This could increase our cybersecurity risk, create data accessibility concerns and make us more susceptible to communication disruptions. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and business operations. For example, the loss of, or inability to access, even temporarily, clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Additionally, healthcare providers have become a frequent target of cybersecurity attacks, and if clinical trial sites suffer a disruption as a result of such an attack, their ability to continue to participate in the trial or to provide trial data to us may be impacted. For example, the Ireland Health Service Executive suffered a

major ransomware and extortion attack in May 2021 that impacted the provision of health services across Ireland. While our clinical trials were not delayed or adversely impacted and our data was not compromised, several of our clinical trial sites were impacted by the attack. Likewise, we rely on third parties for the manufacture of our products and product candidates, including clinical trial supply, and similar events relating to their computer systems could also have a material adverse effect on our business and development programs. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Our business is subject to complex and evolving U.S. and foreign laws and regulations, information security policies and contractual obligations relating to privacy and data protection, including the use, processing, and cross-border transfer of personal information. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, or monetary penalties, and otherwise may harm our business. We receive, generate and store significant and increasing volumes of sensitive information and business-critical information, including employee and personal data, research and development information, commercial information, and business and financial information. Cyber-attacks, breaches, interruptions or other data security incidents could result in legal claims or proceedings, liability under federal or state laws that protect the privacy of personal information, regulatory penalties, significant remediation costs, disrupt key business operations and divert attention of management and key information technology resources. In the United States and Europe, notice of breaches of personal information must be made to affected individuals, and for extensive breaches, notice may need to be made to the media or U.S. state attorneys general or other governmental authorities. Such a notice could harm our reputation and ability to compete.

The United Kingdom's departure from the EU could be costly and difficult to comply with and could harm our business.

The United Kingdom ("UK") formally left the EU on January 31, 2020. We have based in the UK a significant portion of our non-U.S. clinical, regulatory affairs, and pharmacovigilance operations, as well as our European commercial organization. In anticipation of Brexit, we have taken steps to relocate certain activities from the UK in order to remain in compliance, post-Brexit, with certain laws and regulations in the EU. While the regulatory environment in the UK is currently consistent with that of the EU, Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the UK determines which EU laws to replace or replicate. As such, we could be required to comply with regulatory requirements in the UK that are in addition to, or inconsistent with, the regulatory requirements of the EU, resulting in the duplication of certain costs and new challenges to operate in Europe. The full effect of Brexit is uncertain, and consequently, we cannot at this time fully predict what the outcome may have on our business, particularly if our European operations or presence become a more significant part of our business.

Fluctuations in the value of the Euro or UK pound sterling could negatively impact our results of operations and increase our costs.

We generate revenues from sales of Rubraca in the UK and the EU. We also conduct research and development activities in the UK and other European countries and some of the payments for these activities are denominated in Euros and UK pounds sterling. As a result, we are exposed to foreign exchange risk, and our results of operations may be impacted by fluctuations in the exchange rate between the U.S. dollar and the Euro or UK pound sterling, such as the decline in value of the UK pound sterling following the results of the UK's referendum on withdrawal from the EU. We currently have not entered into any foreign currency hedging contracts to reduce the effect of changes in foreign currency exchange rates, and foreign currency hedging is inherently risky and may result in unanticipated losses.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates and other hazardous compounds, and which is expected to include radioactive material contained in FAP-2286. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities, pending use and disposal. We cannot completely eliminate the risk of contamination, which could cause an interruption of our research and development efforts and business operations, injury to our employees and others, environmental damage resulting in costly clean-up

and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently carry biological or hazardous waste insurance coverage.

Environmental, social and governance matters may impact our business and reputation.

Increasingly, in addition to the importance of their financial performance, companies are being judged by their performance on a variety of environmental, social and governance ("ESG") matters, which are considered to contribute to the long-term sustainability of companies' performance.

A variety of organizations measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized. In addition, investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors have publicly emphasized the importance of such ESG measures to their investment decisions. Topics taken into account in such assessments include, among others, the company's efforts and impacts on climate change and human rights, ethics and compliance with law, and the role of the company's board of directors in supervising various sustainability issues. In addition to the topics typically considered in such assessments, in our healthcare industry, issues of the public's ability to access our medicines are of particular importance.

In light of investors' increased focus on ESG matters, there can be no certainty that we will manage such issues successfully, or that we will successfully meet society's expectations as to our proper role. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation and on our business, share price, financial condition, or results of operations, including the sustainability of our business over time.

Climate change, extreme weather events, earthquakes and other natural disasters could adversely affect our business.

In recent years, extreme weather events and changing weather patterns such as storms, flooding, droughts, fires and temperature changes have become more common. As a result, we are potentially exposed to varying natural disaster or extreme weather risks such as hurricanes, tornadoes, fires, droughts or floods, or other events that may result from the impact of climate change on the environment, such as sea level rise. For example, in the event of a major earthquake, we could experience business interruptions, destruction of facilities, and loss of life, all of which could have a material adverse effect on our business, financial condition, or results of operations.

The potential impacts of climate change may also include increased operating costs associated with additional regulatory requirements and investments in reducing energy, water use and greenhouse gas emissions.

Risks Related to Our Intellectual Property

If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold or pursue with respect to our product candidates is threatened, it could threaten our ability to commercialize our product candidates. Further, if we encounter delays in our clinical trials, the

period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office ("U.S. PTO") to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing.

Because Rubraca does not contain a previously approved active ingredient, the Hatch-Waxman Act provides a five-year period of new chemical entity ("NCE") exclusivity following its December 19, 2016 approval during which time generic competitors cannot file an Abbreviated New Drug Application ("ANDA") for a generic version of Rubraca, unless the submission contains a Paragraph IV Certification that one or more patents listed in the Orange Book for Rubraca are invalid, unenforceable or will not be infringed by a proposed ANDA product, in which case the submission may be made four years following the original drug approval. That is, under the provisions of the Hatch-Waxman Act, December 19, 2020 was the earliest date that a generic competitor could submit an ANDA to the FDA requesting permission to market a generic version of Rubraca. Since that time, generic entities have been permitted to file an ANDA for rucaparib with a Paragraph IV certification asserting that one or more patents listed in the Orange Book for Rubraca are either not infringed, invalid, or not enforceable. We have not received any Paragraph IV certification notice letters, and to our knowledge, no ANDA filings for rucaparib have been made to date. If a Paragraph IV Certification is made, the generic company is required to provide a Paragraph IV Notice Letter advising Clovis of the certification. If that occurs, Clovis will have the opportunity to bring a patent infringement action against the generic company. If such a suit is filed within the 45-day period following receipt of the Paragraph IV Notice Letter, the Hatch-Waxman Act provides for a 30-month stay on FDA's ability to grant final approval of the proposed generic product. The 30-month stay generally runs from the date the Paragraph IV Notice Letter is received. However, when a Paragraph IV certification is received during the five-year period of NCE exclusivity following the date of first NDA approval, the thirty-month stay extends from five years after the date that product was first approved. The 30-month stay may be shortened or lengthened, including due to a settlement of a lawsuit, a court order (including a decision by the district court on the merits of the case), or patent expiration. The party filing the ANDA may also counterclaim in the litigation that one or more of our patents are invalid, unenforceable, and/or not infringed. If all of the Orange-Book listed patents were found invalid, enforceable, and/or not infringed, a competing generic product could be marketed prior to expiration of those patents, which would harm our business.

Interference proceedings provoked by third parties or brought by the U.S. PTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Third-party claims of intellectual property infringement may prevent or delay our drug discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including interference, inter parties review and reexamination proceedings before the U.S. PTO or oppositions and other comparable proceedings in foreign jurisdictions. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications, which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtain a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtain a license, limit our uses, or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, limit our uses, pay royalties or redesign our infringing product candidates, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly.

The patent protection, patent prosecution and patent enforcement for some of our product candidates is dependent on third parties.

While we normally seek and gain the right to fully prosecute, maintain and enforce the patents relating to our product candidates, there may be times when platform technology patents that relate to our product candidates are controlled by our licensors. This is the case with the method of use patents licensed under the AstraZeneca license. If AstraZeneca or any of our future licensing partners fail to appropriately prosecute, maintain or enforce, as applicable, patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

If we breach any of the agreements under which we license commercialization rights to our product candidates from third parties, we could lose license rights that are important to our business.

We license the use, development and commercialization rights for all of our product candidates, and may enter into similar licenses in the future. Under each of our existing license agreements we are subject to commercialization and development, diligence obligations, milestone payment obligations, royalty payments and other obligations. If we fail to comply with any of these obligations or otherwise breach our license agreements, including by failing to use commercially reasonable efforts to develop or commercialize the product candidate, our licensing partners may have the right to terminate the license in whole or in part. Generally, the loss of any one of our licenses or other licenses in the future could materially harm our business, prospects, financial condition and results of operations.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

Risks Related to Ownership of our Common Stock, Convertible Senior Notes and Long-term Debt

Our operating results are difficult to predict and may fluctuate. If our operating results are below the expectations of securities analysts or investors, the trading price of our stock could decline.

Our operating results are difficult to predict and may fluctuate significantly from quarter to quarter and year to year. As a result, although we may provide sales guidance for Rubraca from time to time, you should not rely on Rubraca sales results in any period as being indicative of future performance. In addition, such guidance is based on assumptions that may be incorrect or that may change from quarter to quarter, and it may be particularly difficult to correctly forecast sales in indications for which we have recently received marketing approval. Moreover, sales of Rubraca have, on occasion, been below the expectations of securities analysts and investors and have been below prior period sales, and sales of Rubraca in the future may also be below prior period sales, our own guidance and/or the expectations of securities analysts and investors. To the extent that we do not meet any guidance we may give or the expectations of analysts or investors, our stock price may be adversely impacted, perhaps significantly. We believe that our quarterly and annual results of operations may be affected by a variety of factors, including:

- customer ordering patterns for Rubraca, which may vary significantly from period to period;
- the overall level of demand for Rubraca, including the impact of any competitive products and the duration of therapy for patients receiving Rubraca;
- the extent to which coverage and reimbursement for Rubraca is available from government and health administration authorities, private health insurers, managed care programs and other third-party payors;
- our ability to establish or demonstrate to patients and the medical community the safety, efficacy or value of Rubraca and its perceived advantages compared to existing and future therapies in the recurrent ovarian cancer indications and other indications for which Rubraca may receive approval in the future;
- changes in the amount of deductions from gross sales, including government-mandated rebates, chargebacks and discounts that can vary because of changes to the government discount percentage, including increases in the government discount percentage resulting from price increases we have taken or may take in the future, or due to different levels of utilization by entities entitled to government rebates and discounts and changes in patient demographics;
- increases in the scope of eligibility for customers to purchase Rubraca at the discounted government price or to obtain government-mandated rebates on purchases of Rubraca;
- changes in our cost of sales;
- the incidence rate of new patients in Rubraca's approved indications;
- the timing, cost and level of investment in our sales and marketing efforts to support Rubraca sales; and
- the timing, cost and level of investment in our research and development and other activities involving Rubraca, lucitanib and our other product candidates by us or our collaborators.

Further, changes in our operations, such as increased development, manufacturing and clinical trial expenses in connection with our development programs, or our undertaking of additional programs, or business activities, or entry into strategic transactions, including potential future acquisitions of products, technologies or businesses may also cause significant fluctuations in our expenses.

For these and other reasons, it is difficult for us to accurately forecast future sales of Rubraca, operating expenses or future profits or losses. As a result, our operating results in future periods could be below any guidance we may give or the expectations of securities analysts or investors, which could cause the trading price of our common stock to decline, perhaps substantially.

The price of our stock has been, and may continue to be, volatile, and you could lose all or part of your investment.

The trading price of our common stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. During the 12-month period ended December 31, 2021, the price of our common stock on the NASDAQ Global Select Market ranged from $2.70 per share to $10.34 per share. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- our ability and the perception of others as to whether we will be able to continue as a going concern;
- adverse results of regulatory actions or decisions;
- our failure to successfully commercialize our products;
- actual or anticipated adverse results or delays in our clinical trials;
- unanticipated serious safety concerns related to the use of any of our products;
- changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- our dependence on third parties, including CMOS and CROs, as well as our partners that provide us with companion diagnostic products;
- additions or departures of key scientific or management personnel;
- failure to meet or exceed any financial guidance or expectations regarding development milestones that we may provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- overall performance of the equity markets and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- introduction of new products offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- issuances of debt or equity securities and perceptions of our ability to issue additional debt and equity securities to refinance our debt obligations and to fund our operations;
- significant lawsuits, including patent or stockholder litigation;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;

- ineffectiveness of our internal controls;
- general political and economic conditions;
- effects of natural or man-made catastrophic events; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the NASDAQ Global Select Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in these "Risk Factors," could have a dramatic and material adverse effect on the market price of our common stock.

Because our outstanding Notes are convertible into shares of our common stock, volatility or depressed prices of our common stock could have a similar effect on the trading price of our Notes. In addition, the existence of the Notes may encourage short selling in our common stock by market participants because the conversion of the Notes could depress the price of our common stock.

The conversion of some or all of the Notes may dilute the ownership interest of existing stockholders. Holders of the outstanding 2025 Notes are able to convert them at any time prior to the close of business on the business day immediately preceding May 1, 2025. Holders of the outstanding 2024 Notes are able to convert them at any time prior to the close of business on the business day immediately preceding August 1, 2024. Upon conversion, holders of the Notes will receive shares of common stock. Any sales in the public market of shares of common stock issued upon conversion of such Notes could adversely affect the trading price of our common stock. We cannot predict the size of future issuances or the effect, if any, that they may have on the market price of our common stock. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity or convertible debt securities.

Following periods of volatility in a company's stock price, litigation has often been initiated against companies. Following the decline in our stock price related to the rociletinib regulatory update in November 2015, a number of lawsuits have been filed against us and settled. The remaining litigation related to rociletinib are discussed in Part I, Item 3-Legal Proceedings. These proceedings and other similar litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

Our ATHENA clinical trial financing agreement contains a number of covenants and other provisions, which, if violated, could result in the immediate acceleration of our outstanding indebtedness.

Pursuant to our ATHENA clinical trial financing agreement, we are required to repay amounts we borrow from the lenders, capped at specific quarterly amounts, based upon the revenues generated from the sales of Rubraca and other amounts we receive in connection with any out-licensing arrangement or settlement we may enter into with respect to Rubraca. If the total payments made on or prior to December 30, 2025 are less than the total amount borrowed prior to such time, we also would be required to make an additional lump-sum payment to the lenders equal to the amount of that shortfall on that date. Following that date, quarterly payments continue until the lenders have received payments equal to twice the amount borrowed under the financing agreement.

Pursuant to the financing agreement, we have agreed to certain limitations on our operations, including limitations on dividends, stock repurchases and repayments of certain indebtedness, and to certain covenants, including with respect to the conduct of the ATHENA trial. Our obligations under the financing agreement are secured by first priority security interests in all of our assets related to Rubraca, including intellectual property rights.

If an event of default (including a breach or default under, or termination of, any of our material in-license agreements and defaults under our other material indebtedness) occurs under the financing agreement, the lenders have the right to demand immediate repayment of our obligations, which may be as high as twice the amount borrowed thereunder.

In addition, if we do not pay our obligations under the financing agreement when due, including at maturity or upon the occurrence of a liquidity event, which includes a change of control of us or upon demand following the occurrence of an event of default, the lenders would have the right to foreclose on the assets we have pledged as collateral and sell those assets, with the proceeds of the sale being applied to repay the indebtedness.

There can be no assurance that we will not breach the covenants or other terms of, or that an event of default will not occur under, the financing agreement and, if a breach or event of default occurs, there can be no assurance that we will be able to obtain necessary waivers or amendments from the lenders or refinance the related indebtedness on terms we find acceptable, or at all. A default under the financing agreement may also trigger defaults under the indentures governing our senior convertible notes.

As a result, any failure to pay our obligations when due, any breach or default of our covenants or other obligations under the financing agreement, or any other event that allows any lender to demand immediate repayment of borrowings, could have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, the financing agreement may make us less attractive to potential acquirers; and in the event of a change of control of us, the required discharge of the financing agreement out of our available cash or acquisition proceeds would reduce proceeds available to our stockholders.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common stock.

Shares of common stock that are reserved for future issuance under the Notes will become eligible for sale in the public market to the extent permitted by the terms of the Notes. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Pursuant to our equity incentive plan(s), our compensation committee (or its designee) is authorized to grant equity-based incentive awards to our employees, directors and consultants. See Part II, Item 5-Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities for the number of shares of our common stock available for future grant under our 2011 Stock Incentive Plan. Future option and restricted stock unit grants and issuances of common stock under our 2011 Plan may have an adverse effect on the market price of our common stock. In addition, a substantial number of shares of our common stock are reserved for issuance upon conversion of the Notes.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third-party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;

- permitting our board of directors to accelerate the vesting of outstanding option grants upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under Delaware law, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Any provision of our certificate of incorporation or bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock. Additionally, certain provisions of our outstanding Notes could make it more difficult or more expensive for a third party to acquire us. The repurchase price of the Notes must be paid in cash, and this obligation may have the effect of discouraging, delaying or preventing an acquisition of the Company that would otherwise be beneficial to our security holders.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline. In fact, we have had analysts cease coverage of our company in 2021.

There may not be a viable public market for our common stock and as a result it may be difficult for you to sell your shares of our common stock.

Our common stock had not been publicly traded prior to our initial public offering in November 2011. An active trading market for our common stock on the NASDAQ Global Select Market may not be sustained. As a result of these and other factors, you may be unable to resell your shares at a price that is attractive to you or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our principal offices are located at five leased facilities, a 29,256 square foot facility in Boulder, Colorado used primarily for corporate functions, a 24,877 square foot facility in San Francisco, CA used for clinical development operations, a 32,660 square foot facility in Oakland, CA used for clinical development operations and research laboratory space, a 11,805 square foot facility in Cambridge, United Kingdom used for our European regulatory and clinical operations and a 393 square foot facility in Milan, Italy used for commercial activities. These leases expire in January 2023, December 2026, April 2028, July 2029 and November 2022, respectively. We also lease office space in several locations throughout Europe. We believe that our existing facilities are sufficient for our needs for the foreseeable future.

ITEM 3. LEGAL PROCEEDINGS

See Note 12, *Commitments and Contingencies*.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information and Holders

Our common stock trades on the NASDAQ Global Select market under the symbol "CLVS".

On February 15, 2022, there were 26 holders of record of our common stock. The holders of record number do not include a substantially greater number of holders whose shares are held of record in nominee or street name accounts through banks, brokers and/or other financial institutions.

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant. Pursuant to our ATHENA clinical trial financing agreement, we have agreed to limitations on making certain junior payments, including the payment of dividends.

Securities Authorized for Issuance Under Equity Compensation Plans

Equity Compensation Plan Information
As of December 31, 2021

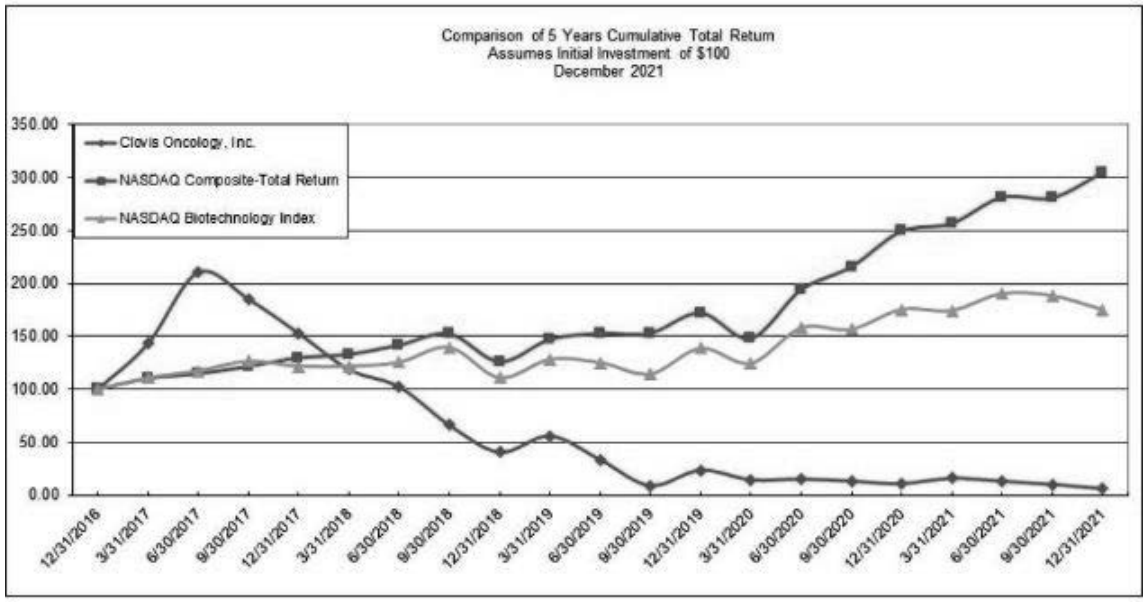
Plan Category	Number of securities to be issued upon exercise of outstanding options and restricted stock (a)	Weighted-average exercise price of outstanding options (b)	Number of securities remaining available for issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders (1) (2)	10,693,461	$ 33.36	9,832,300
Equity compensation plans not approved by security holders	—	—	—
Total	10,693,461	$ 33.36	9,832,300

(1) As of December 31, 2021, 10,970,00 shares were authorized for issuance under our 2020 Stock Incentive Plan (as amended on June 10, 2021, the "2020 Plan"), which became effective on April 22, 2020, which is the date the 2020 Plan was approved by our board of directors.

(2) As of December 31, 2021, 2,783,229 shares were issuable under our 2021 Employee Stock Purchase Plan ("ESPP"), which became effective in April 2021. On February 9, 2022, the Compensation Committee of our Board of Directors amended the ESPP to reduce the total number of shares issuable thereunder from 3,000,000 to 1,000,000 shares.

Performance Graph [(1)]

The following graph shows a comparison from December 31, 2016 through December 31, 2021 of the cumulative total return on an assumed investment of $100 in cash in our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for the NASDAQ Composite Index and the NASDAQ Biotechnology Index assume reinvestment of dividends.



(1) This performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Clovis Oncology, Inc. under the Securities Act of 1933, as amended.

ITEM 6. SELECTED FINANCIAL DATA

Not required.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on acquiring, developing and commercializing innovative anti-cancer agents in the United States, Europe and additional international markets. We target our development programs for the treatment of specific subsets of cancer populations, and simultaneously develop, with partners, for those indications that require them, diagnostic tools intended to direct a compound in development to the population that is most likely to benefit from its use.

Rubraca® is an oral small molecule inhibitor of poly ADP-ribose polymerase ("PARP") marketed in the United States for two indications specific to recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and also an indication specific to metastatic castration-resistant prostate cancer ("mCRPC"). The initial indication received approval from the United States Food and Drug Administration ("FDA") in December 2016 and covers the treatment of adult patients with deleterious *BRCA* (human genes associated with the repair of damaged DNA) mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. Rubraca received a second approval from FDA in April 2018 for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Diagnostic testing is not required for patients to be prescribed Rubraca in this maintenance treatment indication.

In May 2020, the FDA also approved Rubraca for the treatment of adult patients with mCRPC associated with a deleterious *BRCA* mutation (germline and/or somatic) who have been treated previously with androgen receptor-directed therapy and a taxane-based chemotherapy and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. The FDA approved this indication under accelerated approval based on objective response rate and duration of response data from the TRITON2 clinical trial. As an accelerated approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The TRITON3 clinical trial is expected to serve as the confirmatory study for Rubraca's approval in mCRPC as well as the basis for us to seek a potential second-line label expansion. We anticipate the initial data readout from TRITON3 in the second quarter of 2022.

In Europe, the European Commission granted a conditional marketing authorization in May 2018 for Rubraca as monotherapy treatment of adult patients with platinum-sensitive, relapsed or progressive, *BRCA* mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum-based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy. In January 2019, the European Commission granted a variation to the marketing authorization to include the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. With this approval, Rubraca is authorized in Europe for certain patients in the recurrent ovarian cancer maintenance setting regardless of their *BRCA* mutation status. Following successful reimbursement negotiations, Rubraca is marketed in each of Germany, United Kingdom, Italy, France, Spain, the Netherlands and Switzerland.

Beyond our labeled indications, we have a clinical development program underway to further evaluate Rubraca in a variety of solid tumor types, either as monotherapy or in combination with other agents, including the ATHENA Pahse 3 study as part of our ongoing clinical collaboration with Bristol Myers Squibb Company ("Bristol Myers Squibb") to evaluate its immunotherapy OPDIVO® (nivolumab) in combination with Rubraca. We anticipate initial data from two independent readouts for ATHENA during 2022: Rubraca monotherapy versus placebo (ATHENA-MONO) in the second quarter of 2022, with results of the separate analysis of Rubraca in combination with Opdivo (ATHENA-COMBO) anticipated in the fourth quarter of 2022.

The three anticipated data readouts, ATHENA-MONO, ATHENA-COMBO and TRITON3 discussed above, provide the potential to obtain approvals that reach larger patient populations in earlier lines of therapy for ovarian and prostate cancers. Following availability of top-line results from ATHENA-MONO, we plan to file a supplemental New Drug Application ("sNDA") with the FDA and request a variation to the European MAA, and we plan to do the same for the subsequent TRITON3 and ATHENA-COMBO anticipated data readouts, assuming, in each case, that the Phase 3 clinical data is supportive.

The timing for each Phase 3 data readout is contingent upon the occurrence of the protocol-specified progression free survival ("PFS") events, and timing estimates are based on event-based projections.

We hold worldwide rights to Rubraca.

FAP-2286 is our initial product candidate to emerge from our targeted radionuclide therapy collaboration with 3B Pharmaceuticals GmbH ("3BP"). FAP-2286 is a peptide-targeted radionuclide therapy ("PTRT") and imaging agent targeting fibroblast activation protein ("FAP"). PTRT uses cancer cell-targeting peptides to deliver radiation-emitting radionuclides specifically to tumors. Following the clearance by FDA of two INDs submitted in December 2020 to support the use of FAP-2286 as an imaging and treatment agent, we initiated the phase 1 portion of the LuMIERE clinical study in June 2021. LuMIERE is a phase 1/2 study of FAP-2286 labeled with lutetium-177 (^{177}Lu-FAP-2286) evaluating the compound in patients with advanced solid tumors to determine the dose, schedule, and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development program. FAP-2286 labeled with gallium-68 (^{68}Ga-FAP-2286) is being utilized to identify tumors that contain FAP for treatment in this study.

During 2022, we also anticipate the first presentation of phase 1 data from LuMIERE at nuclear medicine-focused meetings, additional presentations of non-clinical data for FAP-2286 and the launch of our combination study program to explore FAP-2286 in combination with other oncology compounds, and in 2023, a potential IND filing of FAP-2286 linked to a FAP-targeted alpha-emitter PTRT.

We hold U.S. and global rights to FAP-2286, excluding Europe (defined to include Russia, Turkey and Israel), where 3BP retains rights.

We are also collaborating with 3BP on a discovery program directed to up to three additional, undisclosed targets for targeted radionuclide therapy, to which we would have global rights for any resulting product candidates.

Lucitanib, our product candidate currently in clinical development, is an investigational, oral, potent angiogenesis inhibitor which inhibits vascular endothelial growth factor receptors 1 through 3 ("VEGFR1-3"), platelet-derived growth factor receptors alpha and beta ("PDGFR α/β") and fibroblast growth factor receptors 1 through 3 ("FGFR1-3"). Lucitanib inhibits the same three pathways as Lenvima® (lenvatinib), which has received an FDA approval for use in certain populations of patients with endometrial cancer in combination with Keytruda® (pembrolizumab), a PD-1 inhibitor. This, together with preclinical data for lucitanib in combination with a PD-1 inhibitor that demonstrated enhanced anti-tumor activity compared to that of single agents, represent a scientific rationale for development of lucitanib in combination with a PD-1 inhibitor, and in February 2019, lucitanib was added to our clinical collaboration with Bristol Myers Squibb. The phase 1b/2 LIO-1 study is evaluating the combination of lucitanib and Opdivo in gynecologic cancers. Interim data from the non-clear cell ovarian cancer expansion cohort were presented at ASCO 2021 and the initial efficacy data do not support further development in non-clear cell ovarian cancer. The remaining three cohorts, which include non-clear cell endometrial, cervical and clear-cell ovarian and endometrial cancers, showed sufficient responses in stage one of each of the cohorts to advance to stage 2. The data from the cervical cohort have been accepted as a plenary presentation at the Society of Gynecologic Oncology (SGO) 2022 Annual Meeting on Women's Cancer in March 2022 and represent encouraging data in this subset of gynecological cancers. However, given the competing priorities, including development of FAP-2286, we have determined that we will not pursue further development of lucitanib in gynecological cancers at this time.

We hold the global (excluding China) development and commercialization rights for lucitanib.

We commenced operations in April 2009. To date, we have devoted substantially all of our resources to identifying and in-licensing product candidates, performing development activities with respect to those product candidates and the general and administrative support of these operations. For the year ended December 31, 2021, we generated $148.8 million product revenue related to sales of Rubraca. We have principally funded our operations using the net proceeds from public offerings of our common stock, convertible senior notes offerings and our financing agreement related to our ATHENA trial.

We have never been profitable and, as of December 31, 2021, we had an accumulated deficit of $2,877.3 million. We incurred net losses of $264.5 million, $369.2 million and $400.4 million for the years ended December 31, 2021, 2020 and 2019, respectively, and had cash and cash equivalents totaling $143.4 million at December 31, 2021.

We have incurred significant net losses since inception and we expect operating losses and negative cash flows to continue for the foreseeable future.

Product License Agreements

For a discussion of our product license agreements, see Note 13, *License Agreements*, in the Notes to Consolidated Financial Statements included in Part II, Item 8, *Financial Statements and Supplementary Data*, of this Annual Report on Form 10-K.

Financial Operations Overview

Revenue

During 2021, we recorded $148.8 million in revenue related to sales of Rubraca. For further discussion of our revenue recognition policy, see "Critical Accounting Policies and Significant Judgments and Estimates" below. Our ability to generate revenue and become profitable depends upon our ability to successfully commercialize products. Any inability on our part to successfully commercialize Rubraca in the United States, Europe and any foreign territories where it may be approved, or any significant delay in such approvals, could have a material adverse impact on our ability to execute upon our business strategy and, ultimately, to generate sufficient revenues from Rubraca to reach or maintain profitability or sustain our anticipated levels of operations.

We supply commercially labeled Rubraca free of charge to eligible patients who qualify due to financial need through our patient assistance program and the majority of these patients are on Medicare. This product is distributed through a separate vendor who administers the program on our behalf. It is not distributed through our specialty distributor and specialty pharmacy network. This product is neither included in the transaction price nor the variable considerations to arrive at product revenue. Manufacturing costs associated with this free product is included in selling, general and administrative expenses. For the year ended December 31, 2021 and 2020, the supply of this free drug was approximately 18% and 17%, respectively, of the overall commercial supply or the equivalent of $24.8 million and $30.4 million, respectively, in commercial value.

Our ability to generate product revenue for the year ended December 31, 2021 was negatively affected by the COVID-19 pandemic, primarily due to the ongoing effect the pandemic has had on oncology treatment and practice, and in particular, in ovarian cancer, resulting in fewer diagnoses and fewer patients going to in-person office visits in the U.S. As a result of the COVID-19 pandemic, our U.S. and European sales forces have had physical access to hospitals, clinics, doctors and pharmacies curtailed and/or have been limited. Our European launches occurred in an environment in which our field-based personnel were not allowed to visit hospitals beginning as early as late February 2020. Similarly, we launched Rubraca for prostate cancer in the U.S beginning in May 2020, but our physical access to hospital, clinics, doctors and pharmacies remains limited. It is difficult to discern or predict any trend in new patient starts due to the unpredictability of the COVID-19 situation and the changing competitive landscape.

Research and Development Expenses

Research and development expenses consist of costs incurred for the development of our product candidates and companion diagnostics, which include:

- license fees and milestone payments related to the acquisition of in-licensed products, which are reported on our Consolidated Statements of Operations and Comprehensive Loss as acquired in-process research and development;
- employee-related expenses, including salaries, benefits, travel and share-based compensation expense;
- expenses incurred under agreements with CROs and investigative sites that conduct our clinical trials;
- the cost of acquiring, developing and manufacturing clinical trial materials;
- costs associated with non-clinical activities and regulatory operations;
- market research and disease education; and
- activities associated with the development of companion diagnostics for our product candidates.

Research and development costs are expensed as incurred. License fees and milestone payments related to in-licensed products and technology are expensed if it is determined that they have no alternative future use. Costs for certain

development activities, such as clinical trials and manufacturing of clinical supply, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors. Our research and development expenses decreased for 2021 compared to 2020. We expect research and development costs to be generally consistent in the full year 2022 compared to 2021.

We did not see material disruption to our clinical trials as a result of the COVID-19 pandemic for the year ended December 31, 2021. However, with the increase in cases of COVID-19 due to the Omicron variant, and the potential for quarantines, unavailability of medical services regarded as non-essential, or reluctance of patients to seek treatment, we may see delays in enrollment during 2022. For example, new patient recruitment in clinical studies, including LuMIERE, may be affected and the conduct of clinical trials may vary by geography as some regions are more adversely affected. Additionally, we may slow or delay enrollment in certain trials to manage expenses.

The following table identifies research and development and acquired in-process research and development costs on a program-specific basis for our products under development. Personnel-related costs, depreciation and share-based compensation are not allocated to specific programs, as they are deployed across multiple projects under development and, as such, are separately classified as personnel and other expenses in the table below.

	Year Ended December 31,		
	2021	2020	2019
		(in thousands)	
Rucaparib Expenses			
Research and development	$ 96,255	$ 159,364	$ 184,617
Rucaparib Total	96,255	159,364	184,617
FAP Expenses			
Research and development	9,230	6,928	3,633
Acquired in-process research and development	5,476	—	9,440
FAP Total	14,706	6,928	13,073
Lucitanib Expenses			
Research and development	9,353	6,860	5,128
Lucitanib Total	9,353	6,860	5,128
Rociletinib Expenses			
Research and development	(176)	(1,089)	1,101
Rociletinib Total	(176)	(1,089)	1,101
Personnel and other expenses	71,940	85,644	88,667
Total	**$ 192,078**	**$ 257,707**	**$ 292,586**

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist principally of salaries and related costs for personnel in executive, commercial, finance, legal, investor relations, human resources and information technology functions. Other general and administrative expenses include facilities expenses, communication expenses, information technology costs, corporate insurance and professional fees for legal, consulting and accounting services. With the FDA approval of Rubraca on December 19, 2016, all sales and marketing expenses associated with Rubraca are included in selling, general and administrative expenses. As a result of the COVID-19 pandemic, our U.S. and European sales forces have had physical access to hospitals, clinics, doctors and pharmacies curtailed and/or have been limited, which have decreased sales and marketing expenses during 2021 and may extend into, and through at least a significant portion, of 2022. In addition, due to increased travel restrictions, quarantines, “work-at-home” and “shelter-in-place” orders and extended shutdown of certain non-essential business in the United States, and European and Asia-Pacific countries, in-person conferences and meetings requiring travel will continue to decrease resulting in a decrease of our selling, general and administrative expenses.

The COVID-19 pandemic has accelerated a preference by oncology practices for more digital programming, including digital, peer-to-peer interactions and reduced in-person promotion. In order to meet these changing preferences, we adopted a hybrid commercial strategy combining increased digital promotion activities, greater online resources and more peer-to-peer interactions with reduced and more targeted in-person promotion. New tools and performance indicators based on this hybrid approach were rolled out during the fourth quarter of 2020. We adopted this strategy in order to better reach customers in the way they want to be reached with the goal of returning to growth,

especially as the ongoing impact of COVID-19 is reduced. The adoption of this strategy also contributed to decreased sales and marketing expenses during the year ended December 31, 2021 due to the reduction in size of our U.S. commercial organization by approximately 45 employees during the fourth quarter of 2020. We expect selling, general and administrative costs to be generally consistent in 2022 as compared to 2021.

Acquired In-Process Research and Development Expenses

Acquired in-process research and development expenses consist of upfront payments to acquire a new drug compound, as well as subsequent milestone payments. Acquired in-process research and development payments are immediately expensed provided that the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no alternative future use. Once regulatory approval is received, payments to acquire rights, and the related milestone payments, are capitalized and the amortization of such assets recorded to product cost of sales.

Other Income and Expense

Other income and expense are primarily comprised of foreign currency gains and losses resulting from transactions with CROs, investigational sites and contract manufacturers where payments are made in currencies other than the U.S. dollar. Other expense also includes interest expense recognized related to our convertible senior notes.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, expenses, revenue and related disclosures. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue, intangible asset impairment, clinical trial accruals and share-based compensation expense. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. We believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We are currently approved to sell Rubraca in the United States and the Europe markets. We distribute our product principally through a limited number of specialty distributor and specialty pharmacy providers, collectively, our customers. Our customers subsequently sell our products to patients and health care providers. Separately, we have arrangements with certain payors and other third parties that provide for government-mandated and privately-negotiated rebates, chargebacks and discounts.

Revenue from product sales are recognized when the performance obligation is satisfied, which is when customers obtain control of our product at a point in time, typically upon delivery. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from price concessions that include rebates, chargebacks, discounts, co-pay assistance, estimated product returns and other allowances that are offered within contracts between us and our customers, health care providers, payors and other indirect customers relating to the sales of our product. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable or a current liability. Where appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which

we are entitled based on the terms of the contract. The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we adjust these estimates, which would affect product revenue and earnings in the period such variances become known.

For the year ended December 31, 2021, we recognized $148.8 million of product revenue. For a complete discussion of the accounting for product revenue, see Note 3, *Revenue Recognition*.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include:

- fees paid to CROs in connection with clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to vendors in connection with non-clinical development activities;
- fees paid to vendors associated with the development of companion diagnostics; and
- fees paid to vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period.

Share-Based Compensation

Determining the amount of share-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. Compensation expense is recognized over the vesting period of the award. Calculating the fair value of share-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the expected dividend yield, price volatility of our common stock, the risk-free interest rate for a period that approximates the expected term of our stock options and the expected term of our stock options. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention to pay cash dividends.

The fair value of stock options for the years ended December 31, 2021, 2020 and 2019 was estimated at the grant date using the following weighted average assumptions for the respective periods:

	Year Ended December 31,		
	2021	2020	2019
Dividend yield	—	—	—
Volatility (a)	101 %	99 %	93 %
Risk-free interest rate (b)	1.30 %	0.49 %	1.67 %
Expected term (years) (c)	6.2	6.0	5.9

(a) *Volatility*: The expected volatility was estimated using our historical data.
(b) *Risk-free interest rate*: The rate is based on the yield on the grant date of a zero-coupon U.S. Treasury bond whose maturity period approximates the option's expected term.
(c) *Expected term*: The expected term of the award was estimated using our historical data.

We recognized share-based compensation expense of approximately $25.5 million, $50.8 million and $54.3 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, the unrecognized share-based compensation expense related to unvested options, adjusted for expected forfeitures, was $8.4 million, which is expected to be recognized over a weighted-average remaining vesting period of 1.5 years. As of December 31, 2021, the unrecognized share-based compensation expense related to RSUs, adjusted for expected forfeitures, was $25.9 million, which is expected to be recognized over an estimated weighted-average remaining vesting period of 1.9 years.

We estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest.

Inventory

Inventories are stated at the lower of cost or estimated net realizable value, on a first-in, first-out ("FIFO") basis. Inventories include active pharmaceutical ingredient ("API"), contract manufacturing costs and overhead allocations. We begin capitalizing incurred inventory related costs upon regulatory approval. Prior to regulatory approval, incurred costs for the manufacture of drugs that could potentially be available to support the commercial launch of our products are recognized as research and development expense.

We regularly analyze our inventory levels for excess quantities and obsolescence (expiration), considering factors such as historical and anticipated future sales compared to quantities on hand and the remaining shelf-life of Rubraca. Rubraca finished goods have a shelf-life of four years from the date of manufacture. We expect to sell the finished goods prior to expiration. The API currently has a shelf-life of five years from the date of manufacture but can be retested at an immaterial cost with no expected reduction in potency, thereby extending its shelf-life as needed. We expect to consume substantially all of the API over a period of approximately seven years based on our long-range sales projections of Rubraca.

We write down inventory that has become obsolete, inventory that has a cost basis in excess of its estimated realizable value and/or inventory in excess of expected sales requirements. Expired finished goods inventory would be disposed of and the related costs would be written off as cost of product revenue. Inventories that are not expected to be consumed within 12 months following the balance sheet date are classified as long-term inventories. Long-term inventories primarily consist of API.

API is currently produced by Lonza. As the API has undergone significant manufacturing specific to its intended purpose at the point it is purchased by us, we classify the API as work-in-process inventory. In addition, we currently manufacture Rubraca finished goods with a single third-party manufacturer. The disruption or termination of the supply of API or the disruption or termination of the manufacturing of our commercial products could have a material adverse effect on our business, financial position and results of operations. API that is written off due to damage and certain costs related to our production train at Lonza are included in Other Operating Expenses in the Consolidated Statements of Operations and Comprehensive Loss.

Inventory used in clinical trials is expensed as research and development expense when it has been identified for such use.

At December 31, 2021, we had $13.7 million of current inventory and $109.8 million of long-term inventory.

Intangible Assets

Definite-lived intangible assets related to capitalized milestones under license agreements are amortized on a straight-line basis over their remaining useful lives, which are estimated to be the remaining patent life. If our estimate of the product's useful life is shorter than the remaining patent life, then a shorter period is used. Amortization expense is recorded as a component of cost of sales in the Consolidated Statements of Operations and Comprehensive Loss.

Intangible assets are evaluated for impairment at least annually in the fourth quarter or more frequently if impairment indicators exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the decision to discontinue the development of a drug, the receipt of additional clinical or nonclinical data regarding our drug candidate or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate, or new information regarding potential sales for the drug. In connection with any impairment assessment, the fair value of the intangible assets as of the date of assessment is compared to the carrying value of the intangible asset. Impairment losses are recognized if the carrying value of an intangible asset is both not recoverable and exceeds its fair value.

Results of Operations

Comparison of the Year Ended December 31, 2021 to the Year Ended December 31, 2020 (in thousands)

	Year ended December 31,					
	2021			2020		
	U.S.	ex-U.S.	Total	U.S.	ex-U.S.	Total
Transaction price	$ 146,357	$ 60,133	$ 206,490	$ 178,427	$ 36,035	$ 214,462
Sales deductions:						
Government rebates and chargebacks	(18,426)	(24,155)	(42,581)	(19,620)	(16,312)	(35,932)
Discounts and fees	(12,258)	(2,894)	(15,152)	(12,548)	(1,460)	(14,008)
Total sales deductions	(30,684)	(27,049)	(57,733)	(32,168)	(17,772)	(49,940)
Product revenue	115,673	33,084	148,757	146,259	18,263	164,522
Operating expenses:						
External cost of sales - product	22,526	10,929	33,455	29,526	6,602	36,128
Cost of sales - intangible asset amortization	2,480	2,891	5,371	2,287	2,890	5,177
Research and development	178,643	7,959	186,602	249,444	8,263	257,707
Selling, general and administrative	104,145	24,255	128,400	139,455	24,439	163,894
Acquired in-process research and development	5,476	—	5,476	—	—	—
Other operating expenses	15,220	—	15,220	3,804	—	3,804
Total expenses	328,490	46,034	374,524	424,516	42,194	466,710
Operating loss	$ (212,817)	$ (12,950)	(225,767)	$ (278,257)	$ (23,931)	(302,188)
Other income (expense):						
Interest expense			(34,103)			(30,508)
Foreign currency loss			(3,177)			(72)
Loss on convertible senior notes conversion			—			(35,075)
Loss on extinguishment of debt			—			(3,277)
Legal settlement loss			(2,325)			—
Other income			444			1,361
Other income (expense), net			(39,161)			(67,571)
Loss before income taxes			(264,928)			(369,759)
Income tax (expense) benefit			404			547
Net loss			$ (264,524)			$ (369,212)

Product Revenue. Total product revenue for the year ended December 31, 2021 decreased compared to the same period in the prior year primarily due to fewer diagnoses and fewer patient starts in the U.S., primarily caused by the ongoing COVID-19 pandemic as there have been fewer patients going to in-person office visits as oncology practices and patients continue to adapt to the impact of the virus and competition from other products on the market, including the impact on second-line maintenance that may result from an increase in first-line maintenance treatment of ovarian cancer.

U.S. product revenue for the year ended December 31, 2021 decreased $30.6 million compared to the same period in the prior year while ex-U.S. product revenue for the year ended December 31, 2021 increased $14.8 million compared to the same period in the prior year. The increase in ex-U.S. product revenue is due to Rubraca being launched in countries in Europe throughout 2019 and 2020.

Product revenue is recorded net of variable considerations comprised of rebates, chargebacks and other discounts. Product revenue for the year ended December 31, 2021 was $115.7 million in the United States and $33.1 million outside of the United States. Total variable considerations represented 28.0% and 23.3% of the transaction price recognized in the year ended December 31, 2021 and 2020, respectively. The increase in variable considerations is primarily due to the European National Health Service rebates related to our sales in Europe and the PHS/340B discounts related to our sales in the U.S. Countries in Europe contract larger government rebates and discounts compared to the U.S. contributing to the overall increase in variable considerations. As European sales increase as a percent of total sales, variable considerations will also increase. The PHS discount related to our U.S. sales has increased as a result of expanding 340B Drug Program purchases by covered entities.

Cost of Sales - Product. Product cost of sales for the year ended December 31, 2021 decreased primarily due to the decrease in product revenue. Product cost of sales primarily relate to manufacturing, freight and royalty costs associated with Rubraca sales in the period.

U.S. product cost of sales for the year ended December 31, 2021 decreased $7.0 million compared to the same period in the prior year due to the decrease in product revenue.

Ex-U.S. product cost of sales for the year ended December 31, 2021 increased $4.3 million compared to the same period in the prior year due to the increase in product revenue.

Cost of Sales – Intangible Asset Amortization. For the year ended December 31, 2021 and 2020, we recognized cost of sales of $5.4 million and $5.2 million, respectively, associated with the amortization of capitalized milestone payments related to the approvals of Rubraca by the FDA and the European Commission.

Research and Development Expenses. Except for activities related to medical research and disease education, research and development expenses are attributable to our U.S. segment. Research and development expenses decreased during the year ended December 31, 2021 compared to the same period in the prior year primarily due to lower research and development costs for Rubraca. The decrease related to our TRITON studies for prostate cancer, our ARIEL and ATHENA studies for ovarian cancer, manufacturing costs, molecular diagnostic costs and personnel costs. These decreases were partially offset by increased costs related to FAP and lucitanib.

Selling, General and Administrative Expenses. Selling, general and administrative expenses decreased during the year ended December 31, 2021 compared to the same period in the prior year due to a $29.6 million decrease in personnel costs, marketing costs and share-based compensation expense primarily due to the reduction in size of our U.S. commercial organization by approximately 45 employees during the fourth quarter of 2020. In addition, we had a $5.6 million decrease in legal expenses. The total decrease in selling, general and administrative expenses mostly related to our U.S. segment while our ex-U.S. selling, general and administrative expenses remained relatively consistent during the year ended December 31, 2021 compared to the same period in the prior year.

Acquired In-Process Research and Development Expenses. In April 2021, we made a milestone payment to 3BP under the license and collaboration agreement of $2.2 million as a result of the FDA's acceptance of the IND for the treatment agent. In September 2021, we made a $3.3 million milestone payment to 3BP under the license and collaboration agreement.

Other Operating Expenses. During the year ended December 31, 2021 and 2020, we recognized other operating expenses related to our production train at Lonza. This expense is related to our fixed facility fee paid to Lonza each quarter, which we recognize as other operating expense when we do not produce inventory at Lonza.

As discussed in Note 12, *Commitments and Contingencies*, we amended this agreement in June 2021, resulting in the derecognition of the lease components recognized under the original agreement. The derecognition of the lease components, payment of $1.1 million to Lonza and derecognition of fixed assets related to our Lonza production train resulted in a loss of $0.3 million, which is included in other operating expenses. Lonza is guaranteeing a minimum

percentage usage of this production train for third parties and Lonza would reduce our fixed facility fee starting in 2023 based on this minimum percentage usage. If Lonza is able to utilize greater than the minimum guaranteed percentage, it will increase the reduction to our fixed facility fee.

Interest Expense. Interest expense increased during the year ended December 31, 2021 compared to the same period in the prior year due to the $9.3 million increase in interest expense under our financing agreement related to our ATHENA trial. This was partially offset by the write off of $4.3 million of unamortized debt issuance costs related to our convertible senior notes transactions that occurred in the prior year. We did not have a similar write off in the current year.

Foreign Currency Loss. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. Transaction losses increased during the year ended December 31, 2021 compared to the same period in the prior year due to significant exchange rate fluctuations that occurred during the year.

Loss on Convertible Senior Notes Conversion. In January 2020, we completed a registered direct offering of an aggregate 17,777,679 shares of our common stock at a price of $9.25 per share. We used the proceeds of the share offering to repurchase an aggregate of $123.4 million principal amount of 2024 Notes (2019 Issuance) in privately negotiated transactions. In addition, we paid customary fees and expenses in connection with the transactions. These transactions resulted in a loss of $7.8 million for the year ended December 31, 2020. There were no similar transactions during the year ended December 31, 2021.

In November 2020, we entered into a privately negotiated exchange and purchase agreement with a holder of our 2024 Notes (2019 Issuance). Pursuant to the agreement, in exchange for approximately $64.8 million aggregate principal amount of 2024 Notes (2019 Issuance) held by the holder, we agreed to issue to the holder a number shares of our common stock (the "Exchanged Shares") utilizing an exchange ratio that is based in part on the daily volume-weighted average prices ("VWAPs") per share of our common stock during a seven-day pricing period following execution of the agreement.

The number of Exchanged Shares was calculated utilizing an exchange ratio that is based in part on the average VWAPs of our common stock (subject to a floor) during a seven-day pricing period beginning on November 5, 2020 and ending on, and including, November 13, 2020. In November 2020, we issued 15,112,848 Exchanged Shares pursuant to the debt exchange transaction. As a result, we recognized a $27.3 million loss on the transactions.

Loss on Extinguishment of Debt. In April 2020, we entered into a privately negotiated exchange agreement with a Holder of our 2021 Notes, pursuant to which we issued to such Holder of the 2021 Notes approximately $36.1 million in additional 2024 Notes (2019 Issuance) of our currently outstanding 2024 Notes (2019 Issuance) in exchange for approximately $32.8 million in aggregate principal of 2021 Notes held by such Holder, which resulted in a $3.3 million loss on extinguishment of debt.

Legal Settlement Loss. During the fourth quarter of 2021, we recorded a charge of $2.3 million in connection with the settlement of the Consolidated Derivative Complaint discussed in Note 12, *Commitments and Contingencies*.

Comparison of the Year Ended December 31, 2020 to the Year Ended December 31, 2019 (in thousands)

	Year ended December 31,					
	2020			2019		
	U.S.	ex-U.S.	Total	U.S.	ex-U.S.	Total
Transaction price	$ 178,427	$ 36,035	$ 214,462	$ 160,450	$ 7,867	$ 168,317
Sales deductions:						
Government rebates and chargebacks	(19,620)	(16,312)	(35,932)	(13,437)	(1,771)	(15,208)
Discounts and fees	(12,548)	(1,460)	(14,008)	(9,826)	(277)	(10,103)
Total sales deductions	(32,168)	(17,772)	(49,940)	(23,263)	(2,048)	(25,311)
Product revenue	146,259	18,263	164,522	137,187	5,819	143,006
Operating expenses:						
Cost of sales - product	29,526	6,602	36,128	28,179	1,747	29,926
Cost of sales - intangible asset amortization	2,287	2,890	5,177	1,956	2,804	4,760
Research and development	249,444	8,263	257,707	275,518	7,628	283,146
Selling, general and administrative	139,455	24,439	163,894	161,132	21,637	182,769
Acquired in-process research and development	—	—	—	9,440	—	9,440
Other operating expenses	3,804	—	3,804	9,711	—	9,711
Total expenses	424,516	42,194	466,710	485,936	33,816	519,752
Operating loss	(278,257)	(23,931)	(302,188)	(348,749)	(27,997)	(376,746)
Other income (expense):						
Interest expense			(30,508)			(19,405)
Foreign currency loss			(72)			(547)
Loss on convertible senior notes conversion			(35,075)			—
(Loss) gain on extinguishment of debt			(3,277)			18,480
Legal settlement loss			—			(26,750)
Other income			1,361			6,342
Other income (expense), net			(67,571)			(21,880)
Loss before income taxes			(369,759)			(398,626)
Income tax benefit (expense)			547			(1,798)
Net loss			$ (369,212)			$ (400,424)

Product Revenue. Product revenue for the year ended December 31, 2020 increased compared to the same period in the prior year primarily due to continued growth in sales of Rubraca, which is approved for sale in the United States and Europe markets. Following successful reimbursement negotiations, Rubraca has been launched in countries in Europe throughout 2019 and 2020. In May 2020, the FDA approved Rubraca as a monotherapy treatment of adult patients with *BRCA1/2*-mutant recurrent, metastatic castrate-resistant prostate cancer and we have launched Rubraca for prostate cancer in the U.S. Product revenue is recorded net of variable considerations comprised of rebates, chargebacks and other discounts. Product revenue for the year ended December 31, 2020 was $146.3 million in the United States and $18.2 million outside of the United States. Variable considerations represented 23.3% and 15.0% of the transaction price recognized in the year ended December 31, 2020 and 2019, respectively. The increase in variable considerations is primarily due to the European National Health Service rebates related to our sales in Europe. Countries in Europe contract larger government rebates and discounts compared to the U.S. contributing to the overall increase in variable considerations. As sales in Europe increase in percentage terms compared to the U.S., variable considerations will also increase. In the United States, PHS chargebacks increased during the year ended December 31, 2020 compared to the prior year. In addition, in the United States, GPO discounts increased during the year ended December 31, 2020 and beginning in January 2020, we began providing payor rebates, which is included in discounts and fees for the year ended December 31, 2020.

Cost of Sales - Product. Product cost of sales for the year ended December 31, 2020 increased primarily due to the increase in product revenue. Product cost of sales primarily relate to manufacturing, freight and royalties costs associated with Rubraca sales in the period.

U.S. product cost of sales for the year ended December 31, 2020 increased $1.3 million compared to the same period in the prior year due to the increase in product revenue.

Ex-U.S. product cost of sales for the year ended December 31, 2020 increased $4.9 million compared to the same period in the prior year due to the increase in product revenue.

Cost of Sales – Intangible Asset Amortization. For the year ended December 31, 2020 and 2019, we recognized cost of sales of $5.2 million and $4.8 million, respectively, associated with the amortization of capitalized milestone payments related to the approvals of Rubraca by the FDA and the European Commission.

Research and Development Expenses. Except for activities related to medical research and disease education, research and development expenses are attributable to our U.S. segment. Research and development expenses decreased during the year ended December 31, 2020 compared to the same period in the prior year primarily due to lower research and development costs for Rubraca. The decrease related to our TRITON studies for prostate cancer, our ARIEL studies for ovarian cancer, discontinuation of our ATLAS study, diagnostic development costs and personnel costs. These decreases were partially offset by increased costs related to our ATHENA combination study with Bristol Myers Squibb's immunotherapy OPDIVO for ovarian cancer. The ATHENA study was initiated in the second quarter of 2018 and we completed target enrollment during the second quarter of 2020. In addition, research and development costs related to FAP and lucitanib have increased since the prior year.

Selling, General and Administrative Expenses. Selling, general and administrative expenses decreased during the year ended December 31, 2020 compared to the same period in the prior year due to a decrease of $13.1 million in marketing costs and $3.2 million in share-based compensation expense. In addition, there was a decrease of $4.0 million in travel due to the COVID-19 pandemic.

U.S. selling, general and administrative expenses decreased $21.7 million during the year ended December 31, 2020 compared to the same period in the prior year due to decreases in marketing costs, share-based compensation expense and a decrease in travel due to the COVID-19 pandemic.

Ex-U.S. selling, general and administrative expenses increased $2.8 million during the year ended December 31, 2020 compared to the same period in the prior year due to the commercial activities related to the Rubraca launches in European countries during 2020.

Acquired In-Process Research and Development Expenses. Upon the signing of the license and collaboration agreement with 3BP in September 2019, we made a $9.4 million upfront payment to 3BP, which is related to our U.S. segment.

Other Operating Expenses. During the year ended December 31, 2020, we recognized other operating expenses related to the write off of some damaged API and certain costs related to our production train at Lonza, which is related to our U.S. segment. We expect these expenses to increase during 2021 related to our fixed facility fee each quarter since we expect to have sufficient inventory and do not plan to produce inventory at Lonza during 2021.

Interest Expense. Interest expense increased during the year ended December 31, 2020 compared to the same period in the prior year due to the May 2019 financing agreement related to our ATHENA trial. In addition, our convertible senior notes transactions during the year resulted in the write off of $4.3 million of unamortized debt issuance costs, which was recorded as interest expense.

Loss/Gain on Extinguishment of Debt. In April 2020, we entered into a privately negotiated exchange agreement with a Holder of our 2021 Notes, pursuant to which we issued to such Holder of the 2021 Notes approximately $36.1 million in additional 2024 Notes (2019 Issuance) of our currently outstanding 2024 Notes (2019 Issuance) in exchange for approximately $32.8 million in aggregate principal of 2021 Notes held by such Holder, which resulted in a $3.3 million loss on extinguishment of debt.

In August 2019, we repurchased $190.3 million aggregate principal amount of our outstanding 2021 Notes and $2.0 million of accrued interest for an aggregate repurchase price of $171.8 million. This repurchase resulted in the write off of $2.0 million in unamortized debt issuance costs and the recognition of $18.5 million gain on extinguishment of debt.

Loss on Convertible Senior Notes Conversion. In January 2020, we completed a registered direct offering of an aggregate 17,777,679 shares of our common stock at a price of $9.25 per share. We used the proceeds of the share offering to repurchase an aggregate of $123.4 million principal amount of 2024 Notes (2019 Issuance) in privately negotiated transactions. In addition, we paid customary fees and expenses in connection with the transactions. These transactions resulted in a loss of $7.8 million for the year ended December 31, 2020.

In November 2020, we entered into a privately negotiated exchange and purchase agreement with a holder of our 2024 Notes (2019 Issuance). Pursuant to the agreement, in exchange for approximately $64.8 million aggregate principal amount of 2024 Notes (2019 Issuance) held by the holder, we agreed to issue to the holder a number shares of our common stock (the "Exchanged Shares") utilizing an exchange ratio that is based in part on the daily volume-weighted average prices ("VWAPs") per share of our common stock during a seven-day pricing period following execution of the agreement.

The number of Exchanged Shares was calculated utilizing an exchange ratio that is based in part on the average VWAPs of our common stock (subject to a floor) during a seven-day pricing period beginning on November 5, 2020 and ending on, and including, November 13, 2020. In November 2020, we issued 15,112,848 Exchanged Shares pursuant to the debt exchange transaction. As a result, we recognized a $27.3 million loss on the transactions.

Legal Settlement Loss. During the second quarter of 2019, we recorded a charge of $26.8 million to settle a complaint filed by Antipodean Domestic Partners.

Other Income. Other income decreased during the year ended December 30, 2020 due to interest income earned on our available-for-sale securities. We did not have available-for-sale securities starting with the quarter ended June 30, 2020 through December 31, 2020.

Liquidity and Capital Resources

Going Concern and Management's Plans

We have incurred significant net losses since inception and have relied on our ability to fund our operations through debt and equity financings. We expect operating losses and negative cash flows to continue for the foreseeable future even with Rubraca now generating revenues. Rubraca revenues have not been consistent in prior quarters, mainly as a result of the impact of COVID-19 and competition from other products on the market, including the impact on second-line maintenance that may result from an increase in first-line maintenance treatment of ovarian cancer, which has made forecasting revenues difficult. In addition to other factors, future Rubraca revenues will depend, in part, on the timing and extent of any recovery from the impacts of COVID-19, with any such recovery expected to take several quarters to have a meaningful impact on our financial results. We do not expect to generate a sufficient amount of Rubraca revenues to finance our cash requirements in the foreseeable future, and which we may never be able to do in sufficient amounts. We require significant cash resources to execute our business plans and we will need to raise additional cash to continue to fund our operating plan. We cannot be certain that additional funding will be available on acceptable terms, or at all especially given that we will need our stockholders to approve an amendment to our certificate of incorporation to increase the number of shares of common stock that we are authorized to issue. The aforementioned factors, which are largely outside of our control, raise substantial doubt about our ability to continue as a going concern within one year from the date of filing of this annual report. The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of asset amounts or the classification of liabilities that might be necessary should we be unable to continue as a going concern within one year after the date the financial statements contained in the Annual Report on Form 10-K are issued.

In the near term, we believe there is some flexibility within our operating plan, particularly with managing certain discretionary expenses, to adjust to variations in our expected Rubraca revenues and the availability and timing of potential sources of financings to meet our working capital requirements. However, based on our current cash, cash equivalents and liquidity available under our ATHENA clinical financing agreement, together with current estimates for revenues generated by sales of Rubraca, we will need to raise additional capital in the near term in order to fund our operating plan for the next 12 months. Our ability to obtain additional financing (including through collaborating and licensing arrangements) will depend on a number of factors, including, among others, our ability to generate positive data from our clinical studies, importantly our ATHENA-MONO clinical trial for which we anticipate initial data in the second quarter of 2022, the condition of the capital markets and the other risks described under *Risk Factors* in this Annual Report on Form 10-K. We expect to finance our operating plan through a combination of public or private equity or debt offerings, collaborations, strategic alliances and other similar licensing arrangements in both the short term and the long term.

We currently have capacity to issue approximately $15.3 million of additional shares of common stock under our previously established ATM Program, assuming the remaining authorized but unissued shares of our common stock are sold at an offering price of $1.69 per share, the closing price of our common stock on the Nasdaq Global Select Market on February 22, 2022. There can be no assurance that we will be able to sell any shares of our common stock under the ATM Program or regarding the price at which we will be able to sell any such shares, and any sales of shares of our common stock under the ATM Program may be at prices that result in additional dilution to existing stockholders of the Company.

It is highly unlikely that we will be able to raise sufficient additional capital through public or private equity offerings (or offerings of securities convertible into our equity securities) until our stockholders approve an amendment to our certificate of incorporation, at our 2022 Annual Meeting of Stockholders, to increase the number of shares of common stock that the Company is authorized to issue. We cannot be certain that our stockholders will approve such a proposal. In the event our stockholders do not approve such a proposal, our ability to raise capital to fund our operations beyond the next 12 months will be significantly limited.

In light of the uncertainty about our ability to raise sufficient capital through potential equity offerings, we will also consider other sources of funding, potentially through incurring further indebtedness or entering into strategic partnerships or licensing arrangements for one or more of our products or product candidates in which we may have to give up certain of our future commercialization rights for interim funding. We are exploring various partnership and licensing arrangements for our products and product candidates outside the U.S., but those will largely depend on our ability to generate positive data from our clinical studies. We cannot be certain that such other sources of funding will be available to us or on acceptable terms or in sufficient amounts to meet our requirements.

In the event that we are unable to raise sufficient additional capital, which is dependent on factors outside of our control, we will need to cut expenses further, including potentially delaying, scaling back or eliminating certain of our pipeline development programs, and undertake a more significant restructuring of our operations, in order to continue as a going concern and fund our committed obligations and working capital requirements. There can be no assurances that we will be able to achieve such a restructuring or that such a restructuring will be successful over the long term to allow us to fund our requirements and our plan to invest sufficient amounts to fund the development of FAP-2286 to its potential.

Sources and Uses of Cash

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Year Ended December 31,		
	2021	2020	2019
		(in thousands)	
Net cash used in operating activities	$ (196,057)	$ (252,728)	$ (323,615)
Net cash (used in) provided by investing activities	(312)	126,328	143,398
Net cash provided by financing activities	100,157	203,644	119,888
Effect of exchange rate changes on cash and cash equivalents	(589)	1,152	286
Net (decrease) increase in cash and cash equivalents	$ (96,801)	$ 78,396	$ (60,043)

Operating Activities

Net cash used in operating activities was lower during the year ended December 31, 2021 compared to the same period in the prior year primarily due to a lower net loss adjusted for non-cash items and changes in components of working capital.

Net cash used in operating activities was lower during the year ended December 31, 2020 compared to the same period in the prior year primarily due to a lower net loss, as adjusted for non-cash items related to our debt transactions. In addition, there was a reduction in payments made for inventory during the period partially offset by payments made for prepaid and accrued research and development expenses.

Investing Activities

There were no significant investing activities during the year ended December 31, 2021 while net cash provided by investing activities for the year ended December 31, 2020 included sales of available-for-sale securities of $144.6 million, partially offset by purchases of available-for-sale securities of $10.0 million and a milestone payment of $8.0 million.

Net cash provided by investing activities for the year ended December 31, 2019 included sales of available-for-sale securities of $622.0 million partially offset by purchases of available-for-sale securities of $459.8 million and milestone payments of $15.8 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 included $116.9 million net proceeds resulting from our "at the market" offerings that occurred during 2021 and $47.5 million proceeds from borrowings under our financing agreement related to our ATHENA trial, partially offset by a $64.4 million payment of our 2021 Notes.

Net cash provided by financing activities for the year ended December 31, 2020 included proceeds of $246.7 million from the issuance of common stock, proceeds of $56.6 million from the issuance of our 2024 Notes (2020 Issuance), partially offset by a $164.4 million payment of our 2024 Notes. In addition, we had $65.1 million proceeds from borrowings under our financing agreement.

Net cash provided by financing activities for the year ended December 31, 2019 included proceeds of $254.9 million from the issuance of our 2024 Notes (2019 Issuance), $32.9 million proceeds from borrowings under our financing agreement and $3.3 million received from employee stock option exercises and issuance of stock under the employee stock purchase plan, partially offset by the $170.0 million extinguishment of a portion of our 2021 Notes.

On May 17, 2021, we entered into a distribution agreement (the "Distribution Agreement") with J.P. Morgan Securities LLC and BofA Securities, Inc., as agents (the "Agents"), pursuant to which we may offer and sell, from time to time, through the Agents, shares of our common stock having an aggregate offering price of up to $75.0 million in transactions that are deemed to be "at the market" offerings as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, including sales made by means of ordinary brokers' transactions, including directly on the Nasdaq Global Select Market or into any other existing trading market for the shares, or sales made to or through a market maker, in block transactions or by any other method permitted by law, including negotiated transactions. Sales may be made at market prices prevailing at the time of a sale or at prices related to prevailing market prices or at negotiated prices. During the period between May 18, 2021 and June 9, 2021, we sold an aggregate of 13,492,231 shares of our common stock under the Distribution Agreement resulting in gross proceeds of $75.0 million and net proceeds to us of $72.5 million, after deducting commissions and offering expenses, effectively closing out sales we may make pursuant to the Distribution Agreement.

The issuance and sale of the shares under the Distribution Agreement were be made pursuant to our effective registration statement on Form S-3 filed with the U.S. Securities and Exchange Commission (the "SEC") on February 25, 2021 (File No. 333-253485) as amended by pre-effective Amendment No. 1 thereto filed with the SEC on May 5, 2021. The offering is described in the Company's prospectus dated May 7, 2021, as supplemented by a prospectus supplement dated May 17, 2021, as filed with the SEC on May 17, 2021. We have used and intend to use the net proceeds of this offering for general corporate purposes, including funding of our development programs, sales and marketing expenses associated with Rubraca, repayment, repurchase or refinance of our debt obligations, payment of milestones pursuant to our license agreements, general and administrative expenses, acquisition or licensing of additional product candidates or businesses and working capital.

On August 16, 2021, we entered into a distribution agreement (the "August Distribution Agreement") with the Agents, pursuant to which we may offer and sell, from time to time, through the Agents, shares of our common stock, having an aggregate offering price of up to $125.0 million in transactions that are deemed to be "at the market" offerings as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, including sales made by means of ordinary brokers' transactions, including directly on the Nasdaq Global Select Market or into any other existing trading market for the shares, or sales made to or through a market maker, in block transactions or by any other method permitted by

law, including privately negotiated transactions. Sales may be made at market prices prevailing at the time of a sale or at prices related to prevailing market prices or at negotiated prices. During the period between August 17, 2021 and September 15, 2021, we sold an aggregate of 9,379,976 shares of our common stock under the August Distribution Agreement resulting in gross proceeds of $43.0 million and net proceeds to us of $41.5 million, after deducting commissions and offering expenses. During the period between November 5, 2021 and November 16, 2021, we sold an aggregate of 731,292 shares of our common stock resulting in gross proceeds of $3.1 million and net proceeds to us of $3.0 million, after deducting commissions and offering expenses. During the period between January 18, 2022 and February 15, 2022, we sold an aggregate of 12,697,044 shares of our common stock resulting in gross proceeds of $28.1 million and net proceeds to us of $27.2 million, after deducting commissions and offering expenses.

The issuance and sale of the shares under the August Distribution Agreement are being made pursuant to our effective registration statement on Form S-3 filed with the SEC on February 25, 2021 (File No. 333-253485) as amended by pre-effective Amendment No. 1 thereto filed with the SEC on May 5, 2021. The offering is described in the Company's prospectus dated May 7, 2021, as supplemented by a prospectus supplement dated August 16, 2021, as filed with the SEC on August 16, 2021. We have used and intend to use the net proceeds of this offering for general corporate purposes, including funding of our development programs, sales and marketing expenses associated with Rubraca, repayment, repurchase or refinance of our debt obligations, payment of milestones pursuant to our license agreements, general and administrative expenses, acquisition or licensing of additional product candidates or businesses and working capital.

Cash Requirements

We expect to incur significant losses for the foreseeable future, as we commercialize Rubraca and expand our selling, general and administrative functions to support the growth in our commercial organization and as we complete research and development activities related to FAP-2286 and lucitanib.

As of December 31, 2021, we had cash and cash equivalents totaling $143.4 million and total current liabilities of $125.2 million. As noted above, subsequent to December 31, 2021, we raised an additional $27.2 million in net proceeds through our "at-the-market" equity offering program.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements. Our future funding requirements will depend on many factors, including but not limited to:

- revenues from the sale of our Rubraca product;
- the number and characteristics of the product candidates, companion diagnostics and indications we pursue;
- the achievement of various development, regulatory and commercial milestones resulting in required payments to partners pursuant to the terms of our license agreements;
- the scope, progress, results and costs of researching and developing our product candidates and related companion diagnostics and conducting clinical and non-clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates and companion diagnostics;
- the cost of commercialization activities, including marketing and distribution costs;
- the cost of manufacturing any of our product candidates we successfully commercialize;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and outcome of such litigation; and
- the timing, receipt and amount of sales, if any, of our products.

The following table summarizes our contractual obligations at December 31, 2021 (in thousands):

	Less than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years	Total
Convertible senior notes	$ —	$ 143,282	$ 300,000	$ —	$ 443,282
Interest on convertible senior notes	10,198	17,727	1,260	—	29,185
Financing agreement (principal and interest) (b)	8,500	68,000	104,718	113,218	294,436
Operating lease commitments	5,224	9,342	9,780	4,952	29,298
Purchase and other commitments (a)	13,152	20,385	9,863	—	43,400
Total	$ 37,074	$ 258,736	$ 425,621	$ 118,170	$ 839,601

(a) On October 3, 2016, we entered into a Manufacturing and Services Agreement (the "Agreement") with a non-exclusive third-party supplier for the production of the active ingredient for Rubraca. Under the terms of the Agreement, we will provide the third-party supplier a rolling forecast for the supply of the active ingredient in Rubraca that will be updated by us on a quarterly basis. We are obligated to order material sufficient to satisfy an initial quantity specified in any forecast. In addition, the third-party supplier constructed, in its existing facility, a production train to manufacture of the Rubraca active ingredient. We are obligated to make scheduled capital program fee payments toward capital equipment and other costs associated with the construction of the production train. Once the facility became operational in October 2018, we were obligated to pay a fixed facility fee each quarter for the duration of the Agreement, which expires on December 31, 2025, unless extended by mutual consent of the parties.

(b) Amounts reflected on the balance sheet and in the table above in respect of the Financing Agreement represent the maximum amounts payable by us to the lenders during the periods indicated. Payments due under our Financing Agreement are based, for the most part, on net sales of Rubraca by us and our licensees. Rubraca sales have not been consistent historically and sales in future periods is difficult to predict. Therefore, expected maturities of our Financing Agreement as of December 31, 2021 are shown based on the quarterly capped amount and certain other mandatory payments set forth in the Financing Agreement. Actual payments may fluctuate and may be less than the amounts reflected in the table above. For a full description of the Financing Agreement and our payment obligations thereunder, see Note 9, *Debt*.

Royalty and License Fee Commitments

Rubraca. We have certain obligations under licensing agreements with third parties contingent upon achieving various development, regulatory and commercial milestones. During 2016 through 2020, we paid Pfizer a total of $82.5 million in milestone payments related to FDA and European Commission approvals received for Rubraca. These milestone payments were recognized as intangible assets and are amortized over the estimated remaining useful life of Rubraca.

We are obligated under the license agreement to use commercially reasonable efforts to develop and commercialize Rubraca and we are responsible for all ongoing development and commercialization costs for Rubraca. We are required to make regulatory milestone payments to Pfizer of up to an additional $8.0 million in aggregate if specified clinical study objectives and regulatory filings, acceptances and approvals are achieved. In addition, we are obligated to make sales milestone payments to Pfizer if specified annual sales targets for Rubraca are met, which relate to annual sales targets of $250.0 million and above, which, in the aggregate, could amount to total milestone payments of $170.0 million, and tiered royalty payments at a mid-teen percentage rate on net sales, with standard provisions for royalty offsets to the extent we need to obtain any rights from third parties to commercialize Rubraca.

FAP. In September 2019, we entered into a global license and collaboration agreement with 3BP to develop and commercialize a PTRT and imaging agent targeting FAP. The lead candidate, designated internally as FAP-2286, is being developed pursuant to a global development plan agreed to by the parties. We are responsible for the costs of all preclinical and clinical development activities described in the plan, including the costs for a limited number of 3BP full-time equivalents and external costs incurred during the preclinical development phase of the collaboration. Upon the signing of the license and collaboration agreement in September 2019, we made a $9.4 million upfront payment to 3BP, which we recognized as acquired in-process research and development expense.

Pursuant to the terms of the FAP agreement, we are required to make additional payments to 3BP for annual technology access fees and upon the achievement of certain development and regulatory milestone events (or on certain

dates, whichever occur earlier). We are also obligated to pay 3BP single- to low-double-digit royalties on net sales of the FAP-targeted therapeutic product and imaging agent, based on the volume of annual net sales achieved. In addition, 3BP is entitled to receive 34% of any consideration, excluding royalties on the therapeutic product, pursuant to any sublicenses we may grant.

We are obligated under the license and collaboration agreement to use diligent efforts to develop FAP-2286 and commercialize a FAP-targeted therapeutic product and imaging agent, and we are responsible for all commercialization costs in our territory. The agreement with 3BP will remain in effect until the expiration of our royalty obligations to 3BP, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, 3BP can terminate the agreement, resulting in a loss of our rights. 3BP also has the right to terminate the agreement under certain circumstances in connection with our change of control in which the acquiring party retains a product competitive with the FAP-targeted therapeutic product or, in the event marketing authorization has not yet been obtained, does not agree to the then-current global development plan.

We submitted two INDs for FAP-2286 for use as imaging and treatment agents in December 2020 to support an initial phase 1 study to determine the dose and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development program. In April 2021, we made a milestone payment to 3BP under the license and collaboration agreement of $2.2 million as a result of the FDA's acceptance of the IND for the treatment agent. In September 2021, we made a $3.3 million milestone payment to 3BP under the license and collaboration agreement.

In February 2020, we finalized the terms of a drug discovery collaboration agreement with 3BP to identify up to three additional, undisclosed targets for PTRT, to which we will obtain global rights for any resulting product candidates. We are responsible for the costs of all preclinical and clinical development activities conducted under the discovery program, including the costs for a limited number of 3BP full-time equivalents and external costs incurred during the discovery and preclinical development phase for each collaboration target. The discovery collaboration agreement was effective December 31, 2019, for which we incurred a $2.1 million technology access fee, which we accrued and recognized as a research and development expense.

Pursuant to the terms of the discovery collaboration agreement, we are required to make additional payments to 3BP for annual technology access fees and upon the achievement of certain development and regulatory milestone events (or on certain dates, whichever occur earlier). We are also obligated to pay 3BP a 6% royalty on net sales of License Products (as defined in the agreement), based on the volume of quarterly net sales achieved.

We are obligated under the discovery collaboration agreement to use diligent efforts to develop and commercialize the product candidates, if any, that result from the discovery program, and we are responsible for all clinical development and commercialization costs. The agreement with 3BP will remain in effect until the expiration of our royalty obligations to 3BP, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, 3BP can terminate the agreement, resulting in a loss of our rights.

Lucitanib. On November 19, 2013, we acquired all of the issued and outstanding capital stock of EOS pursuant to the terms set forth in that certain Stock Purchase Agreement, dated as of November 19, 2013 (the "Stock Purchase Agreement"), by and among the Company, EOS, its shareholders (the "Sellers") and Sofinnova Capital V FCPR, acting in its capacity as the Sellers' representative. Following the acquisition, EOS became a wholly-owned subsidiary of the Company. Under the terms of the Stock Purchase Agreement, in addition to the initial purchase price paid at the time of the closing of the acquisition and other license fees due to Advenchen described below, we will also be obligated to pay to the Sellers a milestone payment of $65.0 million upon obtaining the first NDA approval from the FDA with respect to lucitanib.

In October 2008, Ethical Oncology Science, S.p.A. ("EOS") (now known as Clovis Oncology Italy Srl) entered into an exclusive license agreement with Advenchen Laboratories LLC ("Advenchen") to develop and commercialize lucitanib on a global basis, excluding China.

We are obligated to pay Advenchen tiered royalties at percentage rates in the mid-single digits on net sales of lucitanib, based on the volume of annual net sales achieved. In addition, after giving effect to the first and second

amendments to the license agreement, we are required to pay to Advenchen 25% of any consideration, excluding royalties, we receive from sublicensees, in lieu of the milestone obligations set forth in the agreement. We are obligated under the agreement to use commercially reasonable efforts to develop and commercialize at least one product containing lucitanib, and we are also responsible for all remaining development and commercialization costs for lucitanib.

The license agreement with Advenchen will remain in effect until the expiration of all of our royalty obligations to Advenchen, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, Advenchen can terminate the agreement, resulting in a loss of our rights to lucitanib.

Impact of COVID-19 Pandemic

Our ability to generate product revenue for the year ended December 31, 2021 was negatively affected by the COVID-19 pandemic, primarily due to the ongoing effect the pandemic has had on oncology treatment and practice, and in particular, in ovarian cancer, resulting in fewer diagnoses and fewer patients going to in-person office visits in the U.S. As a result of the COVID-19 pandemic, our U.S. and European sales forces have had physical access to hospitals, clinics, doctors and pharmacies curtailed and/or have been limited. Our European launches occurred in an environment in which our field-based personnel were not allowed to visit hospitals beginning as early as late February 2020. Similarly, we launched Rubraca for prostate cancer in the U.S beginning in May 2020, but our physical access to hospital, clinics, doctors and pharmacies remains limited. It is difficult to discern or predict any trend in new patient starts due to the unpredictability of the COVID-19 situation and the changing competitive landscape.

This curtailment of and/or limited physical access has decreased sales and marketing expenses during 2021 and may extend into, and through at least a significant portion, of 2022. In addition, due to increased travel restrictions, quarantines, "work-at-home" and "shelter-in-place" orders and extended shutdown of certain non-essential business in the United States, and European and Asia-Pacific countries, in-person conferences and meetings requiring travel will decrease, resulting in a decrease of our selling, general and administrative expenses. We believe that we have a sufficient supply of Rubraca and our product candidates to continue our commercial and clinical operations as planned.

The COVID-19 pandemic has accelerated a preference by oncology practices for more digital programming, including digital, peer-to-peer interactions and reduced in-person promotion. In order to meet these changing preferences, we adopted a hybrid commercial strategy combining increased digital promotion activities, greater online resources and more peer-to-peer interactions with reduced and more targeted in-person promotion. New tools and performance indicators based on this hybrid approach were rolled out during the fourth quarter of 2020. We adopted this strategy in order to better reach customers in the way they want to be reached with the goal of returning to growth, especially as the ongoing impact of COVID-19 is reduced.

We did not see material disruption to our clinical trials as a result of the COVID-19 pandemic for the year ended December 31, 2021. However, with the increase in cases of COVID-19 due to the Omicron variant, and the potential for quarantines, unavailability of medical services regarded as non-essential, or reluctance of patients to seek treatment, we may see delays in enrollment during 2022. For example, new patient recruitment in clinical studies, including LuMIERE, may be affected and the conduct of clinical trials may vary by geography as some regions are more adversely affected. Additionally, we may slow or delay enrollment in certain trials to manage expenses.

On March 18, 2020, the Families First Coronavirus Response Act ("FFCR Act"), and on March 27, 2020, the Coronavirus Aid, Relief and Economic Security ("CARES") Act were each enacted in response to the COVID-19 pandemic. The FFCR Act and the CARES Act contain numerous income tax provisions, such as relaxing limitations on the deductibility of interest and the use of net operating losses arising in taxable years beginning after December 31, 2017. On March 11, 2021, President Biden signed an additional coronavirus relief package entitled the American Rescue Plan Act of 2021 ("ARPA"), which included, among other things, provisions relating to stimulus payments to some Americans, extension of several CARES Act relief programs, expansion of the child tax credit, funding for vaccinations and other COVID-19 related assistance programs. The CARES Act, FFCR Act, and the ARPA have not had a material impact on the Company; however, we will continue to examine the impacts that these Acts, as well as any future economic relief legislation, may have on our business.

The trading prices for our common stock and of other biopharmaceutical companies have been highly volatile as a result of the coronavirus pandemic. As a result of this volatility and uncertainties regarding future impact of COVID-19 on our business and operations, we may face difficulties raising capital or may only be able to raise capital on unfavorable terms.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under the rules promulgated by the U.S. Securities and Exchange Commission.

Tax Loss Carryforwards

As of December 31, 2021, we have net operating loss ("NOL") carryforwards of approximately $1.8 billion to offset future federal income taxes. We also have research and development and orphan drug tax credit carryforwards of $259.3 million to offset future federal income taxes. The federal net operating loss carryforwards and research and development and orphan drug tax credit carryforwards expire at various times through 2041.

We believe that a change in ownership as defined under Section 382 of the U.S. Internal Revenue Code occurred as a result of our public offering of common stock completed in April 2012. Future utilization of the federal net operating losses and tax credit carryforwards accumulated from inception to the change in ownership date will be subject to annual limitations to offset future taxable income. It is possible that a change in ownership will occur in the future, which will limit the NOL amounts generated since the last estimated change in ownership. At December 31, 2021, we recorded a 100% valuation allowance against our net deferred tax assets in the U.S. of $873.9 million, as we believe it is more likely than not that the tax benefits will not be fully realized. In the future, if we determine that a portion or all of the tax benefits associated with our tax carryforwards will be realized, net income would increase in the period of determination.

Recently Adopted and Issued Accounting Standards

For a discussion of recently adopted and issued accounting standards, see Note 2, *Summary of Significant Accounting Policies*, in the Notes to Consolidated Financial Statements included in Part II, Item 8, *Financial Statements and Supplementary Data*, of this Annual Report on Form 10-K.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risk related to changes in interest rates. As of December 31, 2021, we had cash, cash equivalents of $143.4 million, consisting of bank demand deposits and money market funds. The primary objectives of our investment policy are to preserve principal and maintain proper liquidity to meet operating needs. Our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available-for-sale securities are subject to interest rate risk and will decline in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair value of our portfolio.

We contract with contract research organizations, investigational sites and contract manufacturers globally where payments are made in currencies other than the U.S. dollar. In addition, on October 3, 2016, we entered into a Manufacturing and Services Agreement with a Swiss company for the production and supply of the active ingredient for Rubraca. Under the terms of this agreement, payments for the supply of the active ingredient in Rubraca as well as scheduled capital program fee payment toward capital equipment and other costs associated with the construction of a production train will be made in Swiss francs. Once the production facility became operational in October 2018, we were obligated to pay a fixed facility fee each quarter for the duration of the agreement, which expires on December 31, 2025.

As of December 31, 2021, $43.4 million of purchase commitments exist under the Swiss Manufacturing and Services Agreement and we are required to remit amounts due in Swiss francs. Due to other variables that may exist, it is difficult to quantify the impact of a particular change in exchange rates. However, we estimate that if the value of the US dollar was to strengthen by 10% compared to the value of Swiss franc as of December 31, 2021, it would decrease the total US

dollar purchase commitment under the Swiss Manufacturing and Services Agreement by approximately $10.6 million. Similarly, a 10% weakening of the US dollar compared to the Swiss franc would increase the total US dollar purchase commitment by approximately $3.3 million.

While we periodically hold foreign currencies, primarily Euro, Pound Sterling and Swiss Franc, we do not use other financial instruments to hedge our foreign exchange risk. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. As of December 31, 2021, and 2020, approximately 4% and 3%, respectively, of our total liabilities were denominated in currencies other than the functional currency.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The financial statements required by this Item are included in Item 15 of this report and are presented beginning on page F-1.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Securities Exchange Act of 1934, as amended ("Exchange Act") is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Principal Financial and Accounting Officer, to allow timely decisions regarding required disclosures. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective.

As of December 31, 2021, our management, with the participation of our Chief Executive Officer and Chief Finance Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Based on this evaluation, our Chief Executive Officer and Chief Finance Officer concluded that, as of December 31, 2021, the design and operation of our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining effective internal control over financial reporting and for the assessment of the effectiveness of internal control over financial reporting. Internal control over financial reporting is a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer and affected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of the consolidated financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or the degree of compliance with the policies or procedures may deteriorate.

As of December 31, 2021, our management, with the participation of our Chief Executive Officer and Chief Finance Officer, assessed the effectiveness of our internal control over financial reporting as defined in Rules 13a-15(f) or 15d-15(f) of the Exchange Act. In making its assessment, management used the criteria established in *Internal Control—Integrated Framework* (2013 framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its assessment, our management determined that, as of December 31, 2021, we maintained effective internal control over financial reporting based on those criteria.

In addition, the effectiveness of our internal control over financial reporting as of December 31, 2021 has been audited by Ernst & Young, LLP, an independent registered public accounting firm.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Clovis Oncology, Inc.

Opinion on Internal Control Over Financial Reporting
We have audited Clovis Oncology, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Clovis Oncology, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2021, and the related notes and our report dated February 23, 2022 expressed an unqualified opinion thereon that included an explanatory paragraph regarding the Company's ability to continue as a going concern.

Basis for Opinion
The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting
A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Denver, Colorado
February 23, 2022

ITEM 9B. OTHER INFORMATION

None.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and is incorporated herein by reference from our definitive proxy statement relating to our 2022 annual meeting of stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, also referred to in this Form 10-K as our 2022 Proxy Statement, which we expect to file with the SEC no later than April 30, 2022.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information regarding our directors, including the audit committee and audit committee financial experts, and executive officers and compliance with Section 16(a) of the Exchange Act will be included in our 2022 Proxy Statement and is incorporated herein by reference.

We have adopted a Code of Business Ethics for all of our directors, officers and employees as required by NASDAQ governance rules and as defined by applicable SEC rules. Stockholders may locate a copy of our Code of Business Ethics on our website at *www.clovisoncology.com* or request a copy without charge from:

Clovis Oncology, Inc.
Attention: Investor Relations
5500 Flatiron Parkway, Suite 100
Boulder, CO 80301

We will post to our website any amendments to the Code of Business Ethics and any waivers that are required to be disclosed by the rules of either the SEC or NASDAQ.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item regarding executive compensation will be included in our 2022 Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item regarding security ownership of certain beneficial owners and management will be included in the 2022 Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

The information required by this item regarding certain relationships and related transactions and director independence will be included in the 2022 Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item regarding principal accounting fees and services will be included in the 2022 Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are being filed as part of this report:

(1) Financial Statements.

Reference is made to the Index to Financial Statements of Clovis Oncology, Inc. appearing on page F-1 of this report.

(2) Financial Statement Schedules.

All financial statement schedules have been omitted because they are not applicable or not required or because the information is included elsewhere in the Financial Statements or the Notes thereto.

(3) Exhibits.

Reference is made to the Index to Exhibits filed as a part of this Annual Report on Form 10-K.

INDEX TO EXHIBITS

Exhibit Number	Exhibit Description
3.1(5)	Amended and Restated Certificate of Incorporation of Clovis Oncology, Inc.
3.2(17)	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Clovis Oncology, Inc.
3.3(5)	Amended and Restated Bylaws of Clovis Oncology, Inc.
3.4(20)	Amendment No. 1 to the Amended and Restated Bylaws of Clovis Oncology, Inc.
4.1(3)	Form of Common Stock Certificate of Clovis Oncology, Inc.
4.2(13)	Indenture dated as of April 19, 2018, by and between Clovis Oncology, Inc. and The Bank of New York Mellon Trust Company, N.A., as Trustee.
4.3(13)	First Supplemental Indenture dated as of April 19, 2018, by and between Clovis Oncology, Inc. and The Bank of New York Mellon Trust Company, N.A.
4.4(18)	Indenture dated as of August 13, 2019, by and between Clovis Oncology, Inc. and The Bank of New York Mellon Trust Company, N.A., as Trustee.
4.5(19)	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934.
4.6(22)	Indenture dated as of November 17, 2020, by and between Clovis Oncology, Inc. and The Bank of New York Mellon Trust Company, N.A., as trustee, relating to the 2024 Notes (2020 Issuance).
10.1*(4)	License Agreement, dated as of June 2, 2011, by and between Clovis Oncology, Inc. and Pfizer Inc.
10.2+(1)	Clovis Oncology, Inc. 2009 Equity Incentive Plan.
10.3+(4)	Clovis Oncology, Inc. 2011 Stock Incentive Plan.
10.4+(26)	Clovis Oncology, Inc. 2020 Stock Incentive Plan.
10.5+(1)	Form of Clovis Oncology, Inc. 2009 Equity Incentive Plan Stock Option Agreement.
10.6+(4)	Form of Clovis Oncology, Inc. 2011 Stock Incentive Plan Stock Option Agreement.
10.7+(21)	Form of Clovis Oncology, Inc. 2020 Stock Incentive Plan Option Agreement.
10.8+(21)	Form of Clovis Oncology, Inc. 2020 Stock Incentive Plan Restricted Stock Unit Agreement.
10.9+(3)	Employment Agreement, dated as of August 24, 2011, by and between Clovis Oncology, Inc. and Patrick J. Mahaffy.
10.10+(3)	Employment Agreement, dated as of August 24, 2011, by and between Clovis Oncology, Inc. and Gillian C. Ivers-Read.
10.11+(1)	Indemnification Agreement, dated as of May 15, 2009, between Clovis Oncology, Inc. and Paul Klingenstein.
10.12+(1)	Indemnification Agreement, dated as of May 15, 2009, between Clovis Oncology, Inc. and James C. Blair.

Exhibit Number	Exhibit Description
10.13+(1)	Indemnification Agreement, dated as of May 15, 2009, between Clovis Oncology, Inc. and Edward J. McKinley.
10.14+(1)	Indemnification Agreement, dated as of May 15, 2009, between Clovis Oncology, Inc. and Thorlef Spickschen.
10.15+(1)	Indemnification Agreement, dated as of May 15, 2009, between Clovis Oncology, Inc. and M. James Barrett.
10.16+(1)	Indemnification Agreement, dated as of May 15, 2009, between Clovis Oncology, Inc. and Brian G. Atwood.
10.17+(1)	Indemnification Agreement, dated as of May 12, 2009, between Clovis Oncology, Inc. and Patrick J. Mahaffy.
10.18+(1)	Indemnification Agreement, dated as of May 12, 2009, between Clovis Oncology, Inc. and Gillian C. Ivers-Read.
10.19+(4)	Clovis Oncology, Inc. 2011 Cash Bonus Plan.
10.20+(2)	Indemnification Agreement, dated as of June 13, 2013, between Clovis Oncology, Inc. and Ginger L. Graham.
10.21+(2)	Indemnification Agreement, dated as of June 13, 2013, between Clovis Oncology, Inc. and Keith Flaherty.
10.22(6)	Stock Purchase Agreement, dated as of November 19, 2013, by and among the Company, EOS, the Sellers listed on Exhibit A thereto and Sofinnova Capital V FCPR, acting in its capacity as the Sellers' Representative.
10.23*(6)	Development and Commercialization Agreement, dated as of October 24, 2008, by and between Advenchen Laboratories LLC and Ethical Oncology Science S.P.A., as amended by the First Amendment, dated as of April 13, 2010 and the Second Amendment, dated as of July 30, 2012.
10.24+(9)	Indemnification Agreement, effective as of August 3, 2015, between Clovis Oncology, Inc. and Lindsey Rolfe.
10.25+(15)	Amended and Restated Employment Agreement, dated as of February 27, 2019, by and between Clovis Oncology UK Limited, Clovis Oncology, Inc. and Dr. Lindsey Rolfe.
10.26+(7)	Indemnification Agreement, dated as of February 17, 2016, between Clovis Oncology, Inc. and Daniel W. Muehl.
10.27+(12)	Employment Agreement, dated as of July 6, 2017, by and between Clovis Oncology, Inc. and Daniel Muehl.
10.28*(8)	First Amendment to License Agreement, between Clovis Oncology, Inc. and Pfizer Inc., dated as of August 30, 2016.
10.29+(10)	Form of Clovis Oncology, Inc. 2011 Stock Incentive Plan RSU Agreement.
10.30*(10)	Manufacturing Services Agreement, by and between Clovis Oncology, Inc. and Lonza Ltd, dated as of October 3, 2016.

Exhibit Number	Exhibit Description
10.31*(11)	Strata Trial Collaboration Agreement, by and between Clovis Oncology, Inc. and Strata Oncology, Inc., dated as of January 30, 2017.
10.32+(14)	Indemnification Agreement, dated as of October 11, 2018, between Clovis Oncology, Inc. and Robert W. Azelby.
10.33+(14)	Indemnification Agreement, dated as of October 11, 2018, between Clovis Oncology, Inc. and Richard A. Fair.
10.34+(15)	Employment Agreement, dated as of July 6, 2017, by and between Clovis Oncology, Inc. and Paul Gross.
10.35+(15)	Indemnification Agreement, dated as of September 9, 2016, between Clovis Oncology, Inc. and Paul E. Gross.
10.36 (16)	Financing Agreement, dated as of May 1, 2019 among Clovis Oncology, Inc., certain of its subsidiaries named therein, as Guarantors, the Lenders from time to time party thereto, and the Administrative Agent party thereto.
10.37(16)	Pledge and Security Agreement, dated as of May 1, 2019 among each of the Grantors party thereto and the Administrative Agent party thereto.
10.38#(23)	License and Collaboration Agreement, dated September 20, 2019 by and between 3B Pharmaceuticals GmbH and Clovis Oncology, Inc.
10.39+(24)	Employment Agreement, dated as of May 4, 2021, by and between Clovis Oncology, Inc. and Thomas C. Harding.
10.40+(24)	Indemnification Agreement, dated as of May 3, 2021, between Clovis Oncology, Inc. and Thomas C. Harding.
10.41+(25)	Indemnification Agreement, dated as of July 12, 2021, between Clovis Oncology, Inc. and Ronit Simantov.
10.42+(26)	Clovis Oncology, Inc. 2021 Employee Stock Purchase Plan.
21.1(27)	List of Subsidiaries of Clovis Oncology, Inc.
23.1	Consent of Independent Registered Public Accounting Firm.
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following materials from Clovis Oncology, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2021 formatted in Inline Extensible Business Reporting Language ("iXBRL"): (i) the Consolidated Statements of Operations and Comprehensive Loss, (ii) the Consolidated Balance Sheets, (iii)

Exhibit Number	Exhibit Description
	the Consolidated Statements of Stockholders' Equity (Deficit), (iv) the Consolidated Statement of Cash Flows and (v) Notes to Consolidated Financial Statements
104	The cover page from Clovis Oncology, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2021 is formatted in iXBRL.

(1) Filed as an exhibit with the Registrant's Registration Statement on Form S-1 (File No. 333-175080) on June 23, 2011.
(2) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on June 14, 2013.
(3) Filed as an exhibit with Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (File No. 333-175080) on August 31, 2011.
(4) Filed as an exhibit with Amendment No. 3 to the Registrant's Registration Statement on Form S-1 (File No. 333-175080) on October 31, 2011.
(5) Filed as an exhibit with the Registrant's Annual Report on Form 10-K on March 15, 2012.
(6) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on November 19, 2013.
(7) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on April 1, 2016.
(8) Filed as an exhibit with the Registrant's Quarterly Report on Form 10-Q on November 4, 2016.
(9) Filed as an exhibit with the Registrant's Annual Report on Form 10-K on February 29, 2016.
(10) Filed as an exhibit with the Registrant's Annual Report on Form 10-K on February 23, 2017.
(11) Filed as an exhibit with the Registrant's Quarterly Report on Form 10-Q on May 4, 2017.
(12) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on July 7, 2017.
(13) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on April 19, 2018.
(14) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on October 12, 2018.
(15) Filed as an exhibit with the Registrant's Annual Report on Form 10-K on February 28, 2019.
(16) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on May 2, 2019.
(17) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on June 6, 2019.
(18) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on August 13, 2019.
(19) Filed as an exhibit with the Registrant's Annual Report on Form 10-K on February 26, 2020.
(20) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on April 16, 2020.
(21) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on June 4, 2020.
(22) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on November 17, 2020.
(23) Filed as an exhibit with the Registrant's Annual Report on Form 10-K on February 25, 2021.
(24) Filed as an exhibit with the Registrant's Quarterly Report on Form 10-Q on May 5, 2021.
(25) Filed as an exhibit with the Registrant's Current Report on Form 8-K (File No. 001-35347) on July 13, 2021.
(26) Filed as an exhibit with the Registrant's Quarterly Report on Form 10-Q on August 4, 2021.
(27) Filed as an exhibit with the Registrant's Quarterly Report on Form 10-Q on November 3, 2021.

\+ Indicates management contract or compensatory plan.

* Confidential treatment has been sought or granted with respect to portions of this exhibit, which portions have been omitted and filed separately with the Securities and Exchange Commission.

\# Confidential portions of this Exhibit were redacted pursuant to Item 601(b)(10) of Regulation S-K and Clovis Oncology, Inc. agrees to furnish supplementary to the Securities and Exchange Commission a copy of any redacted information or omitted schedule and/or exhibit upon request.

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INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Clovis Oncology, Inc.

Opinion on the Financial Statements
We have audited the accompanying consolidated balance sheets of Clovis Oncology, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 23, 2022 expressed an unqualified opinion thereon.

The Company's Ability to Continue as a Going Concern
The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses and negative cash flows from operations since inception, expects to continue to suffer recurring losses and negative cash flows from operations for the foreseeable future, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion
These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters
The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

	Research and development accrual
Description of the Matter	At December 31, 2021, the Company accrued $35.1 million of research and development costs. The completeness and valuation of certain clinical study fees incurred in the Company's accrued research and development costs are subject to risk of estimation uncertainty related to services received and efforts expended. As discussed in Note 2 of the Company's consolidated financial statements, costs for certain

development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred.

Auditing management's accrual of research and development costs was complex and judgmental due to the significant estimation required by management in determining the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. The Company has contracts with multiple contract research organizations ("CROs") that conduct and manage clinical studies on its behalf. The financial terms of these agreements are subject to negotiation and amendment, vary from contract to contract and may result in uneven payment flows.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's accounting for accrued research and development costs. For example, we tested controls over management's review of the research and development accrual calculation, including review of the confirmations from CROs, patient enrollment, sites activated, and the associated contract costs.

To test the estimated accrued research and development, we performed audit procedures that included, among others, assessing methodologies and testing the significant assumptions discussed above, testing the underlying data used by management, and assessing the historical accuracy of management's estimates. We performed inquiries of clinical research managers to understand the status of significant trials, discussed any delays or new developments with the studies to understand the impact of the activity on the accounting for the studies, and confirmed directly with CROs the status of significant cost drivers, such as patient enrollment and site activation.

Sixth Street Financing Agreement

Description of the Matter

As of December 31, 2021, the Company has drawn $147.3 million in principal and incurred $31.2 million in interest expense since inception in relation to the Sixth Street Financing Arrangement. As discussed in Note 10 to the consolidated financial statements, the Company entered into a financing agreement in 2019 through which they plan to borrow amounts required to reimburse actual costs and expenses incurred in clinical trials during each fiscal quarter. They are obligated to make loan payments on a quarterly basis and timing and amount of repayment is dependent on several defined events. The payments are based on a certain percentage of revenues, with a maximum repayment amount each quarter. Therefore, the amounts borrowed, and amounts repaid under the loan are variable. Each period, the Company will determine a new effective interest rate based on the revised estimate of expected remaining cash flows. The new effective interest rate will be used to recognize interest expense prospectively for the remaining periods.

Auditing the financing agreement was complex, and the estimation of future expected cash flows was subjective and was affected by expected future market or economic conditions. The assessment of these terms and future cash flows has a significant effect on the accounting for the agreement.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's accounting for the financing agreement, including management's review of the probabilities of certain conditions or events and certain other assumptions used in the calculation of the interest rate, including the revenue growth rates and projected clinical expenses incurred.

To test the financing agreement, we performed audit procedures that included, among others, testing the assumptions underlying the expected cash flows used to calculate the interest rate, including the revenue growth rates and projected clinical expenses incurred. We compared the assumptions used by management to current industry and economic trends and evaluated whether changes to the Company's customer base or product approvals and other factors would affect the assumptions. We also evaluated management's estimation of the probability of certain conditions or events, which drive certain accounting conclusions. We assessed the historical accuracy of management's estimates and performed sensitivity analyses of the significant assumptions to evaluate the changes in the calculated interest expense that would result from changes in those assumptions.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2009.

Denver, Colorado
February 23, 2022

CLOVIS ONCOLOGY, INC.

Consolidated Statements of Operations and Comprehensive Loss

	Year ended December 31,		
	2021	2020	2019
	(in thousands, except per share amounts)		
Revenues:			
Product revenue	$ 148,757	$ 164,522	$ 143,006
Operating expenses:			
Cost of sales - product	33,455	36,128	29,926
Cost of sales - intangible asset amortization	5,371	5,177	4,760
Research and development	186,602	257,707	283,146
Selling, general and administrative	128,400	163,894	182,769
Acquired in-process research and development	5,476	—	9,440
Other operating expenses	15,220	3,804	9,711
Total expenses	374,524	466,710	519,752
Operating loss	(225,767)	(302,188)	(376,746)
Other income (expense):			
Interest expense	(34,103)	(30,508)	(19,405)
Foreign currency loss	(3,177)	(72)	(547)
Loss on convertible senior notes conversion	—	(35,075)	—
(Loss) gain on extinguishment of debt	—	(3,277)	18,480
Legal settlement loss	(2,325)	—	(26,750)
Other income	444	1,361	6,342
Other income (expense), net	(39,161)	(67,571)	(21,880)
Loss before income taxes	(264,928)	(369,759)	(398,626)
Income tax (expense) benefit	404	547	(1,798)
Net loss	(264,524)	(369,212)	(400,424)
Other comprehensive income (loss):			
Foreign currency translation adjustments, net of tax	874	567	(272)
Net unrealized loss on available-for-sale securities, net of tax	—	(6)	41
Other comprehensive income (loss):	874	561	(231)
Comprehensive loss	$ (263,650)	$ (368,651)	$ (400,655)
Loss per basic and diluted common share:			
Basic and diluted net loss per common share	$ (2.29)	$ (4.38)	$ (7.43)
Basic and diluted weighted average common shares outstanding	115,528	84,307	53,873

See accompanying Notes to Consolidated Financial Statements.

CLOVIS ONCOLOGY, INC.

Consolidated Balance Sheets

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 143,428	$ 240,229
Accounts receivable, net	26,868	26,511
Inventories, net	13,688	30,714
Prepaid research and development expenses	2,397	4,245
Other current assets	11,706	9,130
Total current assets	198,087	310,829
Inventories	109,848	104,123
Property and equipment, net	6,554	12,085
Right-of-use assets, net	19,109	30,438
Intangible assets, net	60,371	65,743
Goodwill	63,074	63,074
Other assets	15,790	19,262
Total assets	$ 472,833	$ 605,554
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 27,308	$ 26,692
Accrued research and development expenses	35,121	43,500
Lease liabilities	3,414	5,330
Convertible senior notes	—	64,198
Borrowings under financing agreement	8,500	—
Other accrued expenses	50,871	45,208
Total current liabilities	125,214	184,928
Long-term lease liabilities - less current portion	19,731	31,640
Convertible senior notes - less current portion	436,772	434,846
Borrowings under financing agreement - less current portion	169,956	110,917
Other long-term liabilities	—	1,971
Total liabilities	751,673	764,302
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, par value $0.001 per share; 10,000,000 shares authorized, no shares issued and outstanding at December 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value per share, 200,000,000 shares authorized at December 31, 2021 and December 31, 2020, respectively; 129,109,543 and 103,699,109 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively	129	104
Additional paid-in capital	2,641,712	2,498,179
Accumulated other comprehensive loss	(43,430)	(44,304)
Accumulated deficit	(2,877,251)	(2,612,727)
Total stockholders' deficit	(278,840)	(158,748)
Total liabilities and stockholders' deficit	$ 472,833	$ 605,554

See accompanying Notes to Consolidated Financial Statements.

CLOVIS ONCOLOGY, INC.

Consolidated Statements of Stockholders' Equity (Deficit)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	
	Shares	Amount	Capital	Income (Loss)	Deficit	Total
			(in thousands, except for share amounts)			
Balance at January 1, 2019	52,797,516	$ 53	$ 2,034,141	$ (44,634)	$ (1,843,091)	$ 146,469
Issuance of common stock under employee stock purchase plan	175,634	—	1,905	—	—	1,905
Exercise of stock options	188,829	—	1,361	—	—	1,361
Issuance of common stock from vesting of restricted stock units	312,304	—	—	—	—	—
Share-based compensation expense	—	—	54,304	—	—	54,304
Legal settlement	1,482,058	2	22,745	—	—	22,747
Net unrealized gain on available-for-sale securities	—	—	—	41	—	41
Foreign currency translation adjustments	—	—	—	(272)	—	(272)
Other financing costs	—	—	(388)	—	—	(388)
Net loss	—	—	—	—	(400,424)	(400,424)
Balance at December 31, 2019	54,956,341	55	2,114,068	(44,865)	(2,243,515)	(174,257)
Issuance of common stock, net of issuance costs	11,090,000	11	83,416	—	—	83,427
Issuance of common stock under employee stock purchase plan	283,588	1	1,419	—	—	1,420
Exercise of stock options	34,599	—	(57)	—	—	(57)
Issuance of common stock from vesting of restricted stock units	1,012,699	1	(1)	—	—	—
Share-based compensation expense	—	—	50,794	—	—	50,794
Net unrealized gain on available-for-sale securities	—	—	—	(6)	—	(6)
Foreign currency translation adjustments	—	—	—	567	—	567
Convertible senior notes conversion	36,321,882	36	248,599	—	—	248,635
Other financing costs	—	—	(59)	—	—	(59)
Net loss	—	—	—	—	(369,212)	(369,212)
Balance at December 31, 2020	103,699,109	104	2,498,179	(44,304)	(2,612,727)	(158,748)
Issuance of common stock, net of issuance costs	23,603,499	24	116,900	—	—	116,924
Issuance of common stock under employee stock purchase plan	375,153	—	1,146	—	—	1,146
Exercise of stock options	7,087	—	35	—	—	35
Issuance of common stock from vesting of restricted stock units	1,424,695	1	(1)	—	—	—
Share-based compensation expense	—	—	25,453	—	—	25,453
Foreign currency translation adjustments	—	—	—	874	—	874
Net loss	—	—	—	—	(264,524)	(264,524)
Balance at December 31, 2021	129,109,543	$ 129	$ 2,641,712	$ (43,430)	$ (2,877,251)	$ (278,840)

See accompanying Notes to Consolidated Financial Statements.

CLOVIS ONCOLOGY, INC.

Consolidated Statements of Cash Flows

	Year ended December 31,		
	2021	2020	2019
		(in thousands)	
Operating activities			
Net loss	$ (264,524)	$ (369,212)	$ (400,424)
Adjustments to reconcile net loss to net cash used in operating activities:			
Share-based compensation expense	25,453	50,794	54,304
Depreciation and amortization	8,496	8,198	7,768
Amortization of premiums and discounts on available-for-sale securities	—	(174)	(1,521)
Amortization of debt issuance costs	2,430	2,672	2,858
Write-off of debt issuance costs related to convertible senior notes transactions	—	4,345	—
Loss on convertible senior notes conversion	—	35,075	—
Loss on extinguishment of debt	—	3,277	(18,480)
Legal settlement loss	—	—	22,747
Other	1,817	340	804
Changes in operating assets and liabilities:			
Accounts receivable	(746)	(5,407)	(7,518)
Inventory	12,574	5,321	(26,160)
Prepaid and accrued research and development expenses	(5,088)	(8,313)	23,233
Other operating assets and liabilities	(2,941)	10,831	(6,837)
Accounts payable	736	(5,852)	12,289
Other accrued expenses	25,736	15,377	13,322
Net cash used in operating activities	(196,057)	(252,728)	(323,615)
Investing activities			
Purchases of property and equipment	(312)	(354)	(3,290)
Proceeds from sale of property and equipment	—	—	275
Purchases of available-for-sale securities	—	(9,962)	(459,835)
Sales of available-for-sale securities	—	144,644	621,998
Acquired in-process research and development - milestone payment	—	(8,000)	(15,750)
Net cash (used in) provided by investing activities	(312)	126,328	143,398
Financing activities			
Proceeds from sale of common stock, net of issuance costs	116,924	246,668	—
Proceeds from issuance of convertible senior notes, net of issuance costs	—	56,619	254,879
Payment of convertible senior notes	(64,418)	(164,443)	—
Extinguishment of convertible senior notes	—	—	(169,853)
Proceeds from borrowings under financing agreement	47,462	65,119	32,871
Proceeds from the exercise of stock options and employee stock purchases	1,182	1,362	3,266
Payments on finance leases	(780)	(1,470)	(1,115)
Payments on other long-term liabilities	(213)	(211)	(160)
Net cash provided by financing activities	100,157	203,644	119,888
Effect of exchange rate changes on cash and cash equivalents	(589)	1,152	286
(Decrease) increase in cash and cash equivalents	(96,801)	78,396	(60,043)
Cash and cash equivalents at beginning of period	240,229	161,833	221,876
Cash and cash equivalents at end of period	$ 143,428	$ 240,229	$ 161,833
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 11,071	$ 12,075	$ 10,515
Non-cash investing and financing activities:			
Vesting of restricted stock units	$ 10,019	$ 7,493	$ 5,442

See accompanying Notes to Consolidated Financial Statements.

1. Nature of Business

We are a biopharmaceutical company focused on acquiring, developing and commercializing innovative anti-cancer agents in the United States, Europe and additional international markets. We target our development programs for the treatment of specific subsets of cancer populations, and simultaneously develop, with partners, for those indications that require them, diagnostic tools intended to direct a compound in development to the population that is most likely to benefit from its use.

Rubraca® is an oral small molecule inhibitor of poly ADP-ribose polymerase ("PARP") marketed in the United States for two indications specific to recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and also an indication specific to metastatic castration-resistant prostate cancer ("mCRPC"). The initial indication received approval from the United States Food and Drug Administration ("FDA") in December 2016 and covers the treatment of adult patients with deleterious *BRCA* (human genes associated with the repair of damaged DNA) mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. Rubraca received a second approval from FDA in April 2018 for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Diagnostic testing is not required for patients to be prescribed Rubraca in this maintenance treatment indication.

In May 2020, the FDA also approved Rubraca for the treatment of adult patients with mCRPC associated with a deleterious *BRCA* mutation (germline and/or somatic) who have been treated previously with androgen receptor-directed therapy and a taxane-based chemotherapy and selected for therapy based on an FDA-approved companion diagnostic for Rubraca. The FDA approved this indication under accelerated approval based on objective response rate and duration of response data from the TRITON2 clinical trial. As an accelerated approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The TRITON3 clinical trial is expected to serve as the confirmatory study for Rubraca's approval in mCRPC as well as the basis for us to seek a potential second-line label expansion. We anticipate the initial data readout from TRITON3 in the second quarter of 2022.

In Europe, the European Commission granted a conditional marketing authorization in May 2018 for Rubraca as monotherapy treatment of adult patients with platinum-sensitive, relapsed or progressive, *BRCA* mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum-based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy. In January 2019, the European Commission granted a variation to the marketing authorization to include the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. With this approval, Rubraca is authorized in Europe for certain patients in the recurrent ovarian cancer maintenance setting regardless of their *BRCA* mutation status. Following successful reimbursement negotiations, Rubraca is marketed in each of Germany, United Kingdom, Italy, France, Spain, the Netherlands and Switzerland.

Beyond our labeled indications, we have a clinical development program underway to further evaluate Rubraca in a variety of solid tumor types, either as monotherapy or in combination with other agents, including the ATHENA Phase 3 study as part of our ongoing clinical collaboration with Bristol Myers Squibb Company ("Bristol Myers Squibb") to evaluate its immunotherapy OPDIVO® (nivolumab) in combination with Rubraca. We anticipate initial data from two independent readouts for ATHENA during 2022: Rubraca monotherapy versus placebo (ATHENA-MONO) in the second quarter of 2022, with results of the separate analysis of Rubraca in combination with Opdivo (ATHENA-COMBO) anticipated in the fourth quarter of 2022.

The three anticipated data readouts, ATHENA-MONO, ATHENA-COMBO and TRITON3 discussed above, provide the potential to obtain approvals that reach larger patient populations in earlier lines of therapy for ovarian and prostate cancers. Following availability of top-line results from ATHENA-MONO, we plan to file a supplemental New Drug

Application ("sNDA") with the FDA and request a variation to the European MAA, and we plan to do the same for the subsequent TRITON3 and ATHENA-COMBO anticipated data readouts, assuming, in each case, that the Phase 3 clinical data is supportive.

The timing for each Phase 3 data readout is contingent upon the occurrence of the protocol-specified progression free survival ("PFS") events, and timing estimates are based on event-based projections.

We hold worldwide rights to Rubraca.

FAP-2286 is our initial product candidate to emerge from our targeted radionuclide therapy collaboration with 3B Pharmaceuticals GmbH ("3BP"). FAP-2286 is a peptide-targeted radionuclide therapy ("PTRT") and imaging agent targeting fibroblast activation protein ("FAP"). PTRT uses cancer cell-targeting peptides to deliver radiation-emitting radionuclides specifically to tumors. Following the clearance by FDA of two INDs submitted in December 2020 to support the use of FAP-2286 as an imaging and treatment agent, we initiated the phase 1 portion of the LuMIERE clinical study in June 2021. LuMIERE is a phase 1/2 study of FAP-2286 labeled with lutetium-177 (^{177}Lu-FAP-2286) evaluating the compound in patients with advanced solid tumors to determine the dose, schedule, and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development program. FAP-2286 labeled with gallium-68 (^{68}Ga-FAP-2286) is being utilized to identify tumors that contain FAP for treatment in this study.

During 2022, we also anticipate the first presentation of phase 1 data from LuMIERE at nuclear medicine-focused meetings, additional presentations of non-clinical data for FAP-2286 and the launch of our combination study program to explore FAP-2286 in combination with other oncology compounds, and in 2023, a potential IND filing of FAP-2286 linked to a FAP-targeted alpha-emitter PTRT.

We hold U.S. and global rights to FAP-2286, excluding Europe (defined to include Russia, Turkey and Israel), where 3BP retains rights.

We are also collaborating with 3BP on a discovery program directed to up to three additional, undisclosed targets for targeted radionuclide therapy, to which we would have global rights for any resulting product candidates.

Lucitanib, our product candidate currently in clinical development, is an investigational, oral, potent angiogenesis inhibitor which inhibits vascular endothelial growth factor receptors 1 through 3 ("VEGFR1-3"), platelet-derived growth factor receptors alpha and beta ("PDGFR α/β") and fibroblast growth factor receptors 1 through 3 ("FGFR1-3"). Lucitanib inhibits the same three pathways as Lenvima® (lenvatinib), which has received an FDA approval for use in certain populations of patients with endometrial cancer in combination with Keytruda® (pembrolizumab), a PD-1 inhibitor. This, together with preclinical data for lucitanib in combination with a PD-1 inhibitor that demonstrated enhanced anti-tumor activity compared to that of single agents, represent a scientific rationale for development of lucitanib in combination with a PD-1 inhibitor, and in February 2019, lucitanib was added to our clinical collaboration with Bristol Myers Squibb. The phase 1b/2 LIO-1 study is evaluating the combination of lucitanib and Opdivo in gynecologic cancers. Interim data from the non-clear cell ovarian cancer expansion cohort were presented at ASCO 2021 and the initial efficacy data do not support further development in non-clear cell ovarian cancer. The remaining three cohorts, which include non-clear cell endometrial, cervical and clear-cell ovarian and endometrial cancers, showed sufficient responses in stage one of each of the cohorts to advance to stage 2. The data from the cervical cohort have been accepted as a plenary presentation at the Society of Gynecologic Oncology (SGO) 2022 Annual Meeting on Women's Cancer in March 2022 and represent encouraging data in this subset of gynecological cancers. However, given the competing priorities, including development of FAP-2286, we have determined that we will not pursue further development of lucitanib in gynecological cancers at this time.

We hold the global (excluding China) development and commercialization rights for lucitanib.

Going Concern and Management Plans

We have incurred significant net losses since inception and have relied on our ability to fund our operations through debt and equity financings. We expect operating losses and negative cash flows to continue for the foreseeable future even with Rubraca now generating revenues. Rubraca revenues have not been consistent in prior quarters, mainly as a result of the impact of COVID-19 and competition from other products on the market, including the impact on second-

line maintenance that may result from an increase in first-line maintenance treatment of ovarian cancer, which has made forecasting revenues difficult. In addition to other factors, future Rubraca revenues will depend, in part, on the timing and extent of any recovery from the impacts of COVID-19, with any such recovery expected to take several quarters to have a meaningful impact on our financial results. We do not expect to generate a sufficient amount of Rubraca revenues to finance our cash requirements in the foreseeable future, and which we may never be able to do in sufficient amounts. We require significant cash resources to execute our business plans and we will need to raise additional cash to continue to fund our operating plan. We cannot be certain that additional funding will be available on acceptable terms, or at all especially given that we will need our stockholders to approve an amendment to our certificate of incorporation to increase the number of shares of common stock that we are authorized to issue. The aforementioned factors, which are largely outside of our control, raise substantial doubt about our ability to continue as a going concern within one year from the date of filing of this annual report.

In the near term, we believe there is some flexibility within our operating plan, particularly with managing certain discretionary expenses, to adjust to variations in our expected Rubraca revenues and the availability and timing of potential sources of financings to meet our working capital requirements. However, based on our current cash, cash equivalents and liquidity available under our ATHENA clinical financing agreement, together with current estimates for revenues generated by sales of Rubraca, we will need to raise additional capital in the near term in order to fund our operating plan for the next 12 months. Our ability to obtain additional financing (including through collaborating and licensing arrangements) will depend on a number of factors, including, among others, our ability to generate positive data from our clinical studies, importantly our ATHENA-MONO clinical trial for which we anticipate initial date in the second quarter of 2022, the condition of the capital markets and the other risks described in under Risk Factors in this Annual Report on Form 10-K. We expect to finance our operating plan through a combination of public or private equity or debt offerings, collaborations, strategic alliances and other similar licensing arrangements in both the short term and the long term.

We currently have capacity to issue approximately $15.3 million of additional shares of common stock under our previously established ATM Program, assuming the remaining authorized but unissued shares of our common stock are sold at an offering price of $1.69 per share, the closing price of our common stock on the Nasdaq Global Select Market on February 22, 2022. There can be no assurance that we will be able to sell any shares of our common stock under the ATM Program or regarding the price at which we will be able to sell any such shares, and any sales of shares of our common stock under the ATM Program may be at prices that result in additional dilution to existing stockholders of the Company.

It is highly unlikely that we will be able to raise sufficient additional capital through public or private equity offerings (or offerings of securities convertible into our equity securities) until our stockholders approve an amendment to our certificate of incorporation, at our 2022 Annual Meeting of Stockholders, to increase the number of shares of common stock that the Company is authorized to issue. We cannot be certain that our stockholders will approve such a proposal. In the event our stockholders do not approve such a proposal, our ability to raise capital to fund our operations beyond the next 12 months will be significantly limited.

In light of the uncertainty about our ability to raise sufficient capital through potential equity offerings, we will also consider other sources of funding, potentially through incurring further indebtedness or entering into strategic partnerships or licensing arrangements for one or more of our products or product candidates in which we may have to give up certain of our future commercialization rights for interim funding. We are exploring various partnership and licensing arrangements for our products and product candidates outside the U.S., but those will largely depend on our ability to generate positive data from our clinical studies. We cannot be certain that such other sources of funding will be available to us or on acceptable terms or in sufficient amounts to meet our requirements.

In the event that we are unable to raise sufficient additional capital, which is dependent on factors outside of our control, we will need to cut expenses further, including potentially delaying, scaling back or eliminating certain of our pipeline development programs, and undertake a more significant restructuring of our operations, in order to continue as a going concern and fund our committed obligations and working capital requirements. If an event of default were to occur under our ATHENA Clinical Financing Agreement, or if an event of default were to be determined to be probable, we would classify all our obligations that become due and payable thereunder as current liabilities. There can be no assurances that we will be able to achieve such a restructuring or that such a restructuring will be successful over the

long term to allow us to fund our requirements and our plan to invest sufficient amounts to fund the development of FAP-2286 to its potential.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP"). The consolidated financial statements include our accounts and our wholly-owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation. The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of asset amounts or the classification of liabilities that might be necessary should we be unable to continue as a going concern within one year after the date these financial statements are issued.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and revenue and related disclosures. On an ongoing basis, we evaluate our estimates, including estimates related to revenue deductions, intangible asset impairment, clinical trial accruals and share-based compensation expense. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Revenue Recognition

We are currently approved to sell Rubraca in the United States and the Europe markets. We distribute our product principally through a limited number of specialty distributor and specialty pharmacy providers, collectively, our customers. Our customers subsequently sell our products to patients and health care providers. Separately, we have arrangements with certain payors and other third-parties that provide for government-mandated and privately-negotiated rebates, chargebacks and discounts. See Note 3, *Revenue Recognition*.

Cost of Sales – Product

Product cost of sales consists primarily of materials, third-party manufacturing costs as well as freight and royalties owed to our licensing partners for Rubraca sales.

Cost of Sales – Intangible Asset Amortization

Cost of sales for intangible asset amortization consists of the amortization of capitalized milestone payments made to our licensing partners upon FDA approval of Rubraca. Milestone payments are amortized on a straight-line basis over the estimated remaining patent life of Rubraca.

Fair Value of Financial Instruments

Cash and cash equivalents are carried at fair value. Financial instruments, including other current assets and accounts payable, are carried at cost, which approximates fair value given their short-term nature (see Note 5, *Fair Value Measurements*).

Cash and Cash Equivalents

We consider all highly liquid investments with original maturities at the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents include bank demand deposits and money market funds that invest primarily in certificate of deposits, commercial paper and U.S. government and U.S. government agency obligations.

Accounts Receivable

We provide an allowance for credit losses based on experience and specifically identified risks. Accounts receivable are charged off against the allowance when we determine that recovery is unlikely and we cease collection efforts.

Inventory

Inventories are stated at the lower of cost or estimated net realizable value, on a first-in, first-out ("FIFO") basis. Inventories include active pharmaceutical ingredient ("API"), contract manufacturing costs and overhead allocations. We begin capitalizing incurred inventory related costs upon regulatory approval. Prior to regulatory approval, incurred costs for the manufacture of the drugs that could potentially be available to support the commercial launch of our products are recognized as research and development expense.

We regularly analyze our inventory levels for excess quantities and obsolescence (expiration), considering factors such as historical and anticipated future sales compared to quantities on hand and the remaining shelf-life of Rubraca. Rubraca finished goods have a shelf-life of four years from the date of manufacture. We expect to sell the finished goods prior to expiration. The API currently has a shelf-life of five years from the date of manufacture but can be retested at an immaterial cost with no expected reduction in potency, thereby extending its shelf-life as needed. We expect to consume substantially all of the API over a period of approximately seven years based on our long-range sales projections of Rubraca.

We write down finished goods inventory that has become obsolete, inventory that has a cost basis in excess of its estimated realizable value and/or inventory in excess of expected sales requirements. Expired inventory would be disposed of and the related costs would be written off as cost of product revenue. Inventories that are not expected to be consumed within 12 months following the balance sheet date are classified as long-term inventories. Long-term inventories primarily consist of API.

API is currently produced by Lonza. As the API has undergone significant manufacturing specific to its intended purpose at the point it is purchased by us, we classify the API as work-in-process inventory. In addition, we currently manufacture Rubraca finished goods with a single third-party manufacturer. The disruption or termination of the supply of API or the disruption or termination of the manufacturing of our commercial products could have a material adverse effect on our business, financial position and results of operations. API that is written off due to damage and certain costs related to our production train at Lonza are included in Other Operating Expenses on the Consolidated Statements of Operations and Comprehensive Loss.

Inventory used in clinical trials is expensed as research and development expense when it has been identified for such use.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets. Equipment purchased for use in manufacturing and clinical trials is evaluated to determine whether the equipment is solely beneficial for a drug candidate in the development stage or whether it has an alternative use. Equipment with an alternative use is capitalized. Leased assets meeting certain finance lease criteria are capitalized and the present value of the related lease payments is recorded as a liability. Assets under finance lease arrangements are depreciated using the straight-line method over the estimated useful lives. Leasehold improvements are amortized over the economic life of the asset or the lease term, whichever is shorter. Maintenance and repairs are expensed as incurred. The estimated useful lives of our capitalized assets are as follows:

	Estimated Useful Life
Computer hardware and software	3 to 5 years
Leasehold improvements	6 years
Laboratory, manufacturing and office equipment	5 to 7 years
Furniture and fixtures	10 years

Long-Lived Assets

We review long-lived assets for impairment when events or changes in circumstances indicate that the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the assets' book value to future net undiscounted cash flows that the assets are expected to generate. If the carrying value of the assets exceed their future net undiscounted cash flows, an impairment charge is recognized for the amount by which the carrying value of the assets exceeds the fair value of the assets.

Intangible Assets, Net

Definite-lived intangible assets related to capitalized milestones under license agreements are amortized on a straight-line basis over their remaining useful lives, which are estimated to be the remaining patent life. If our estimate of the product's useful life is shorter than the remaining patent life, then a shorter period is used. Amortization expense is recorded as a component of cost of sales on the Consolidated Statements of Operations and Comprehensive Loss.

Intangible assets are evaluated for impairment at least annually in the fourth quarter or more frequently if impairment indicators exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the decision to discontinue the development of a drug, the receipt of additional clinical or nonclinical data regarding our drug candidate or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate, or new information regarding potential sales for the drug. In connection with any impairment assessment, the fair value of the intangible assets as of the date of assessment is compared to the carrying value of the intangible asset. Impairment losses are recognized if the carrying value of an intangible asset is both not recoverable and exceeds its fair value.

Goodwill

Goodwill was recorded as a result of the EOS acquisition in November 2013. Goodwill represents the excess of the purchase price over the fair value of net assets acquired in a business combination accounted for under the acquisition method of accounting and is not amortized, but is subject to impairment testing at least annually in the fourth quarter or when a triggering event is identified that could indicate a potential impairment. We are organized as two reporting units based on our operating segments, U.S. and ex-U.S. We determined that our goodwill was allocated to the U.S. reporting unit and performed impairment testing by assessing qualitative factors to determine whether it is more likely than not (that is, a likelihood of more than 50 percent) that the fair value of a reporting unit is less than its carrying amount. Based on our qualitative assessment and that the U.S. reporting unit had a negative carrying value, we determined that it is not more likely than not that the fair value of a reporting unit is less than its carrying amount. Therefore, the quantitative goodwill impairment test is not necessary. There is no goodwill impairment as of December 31, 2021.

Other Current Assets

Other current assets are comprised of the following (in thousands):

	December 31, 2021	December 31, 2020
Prepaid insurance	$ 794	$ 782
Prepaid IT	769	753
Prepaid variable considerations	1,336	1,191
Prepaid expenses - other	1,936	2,193
Value-added tax ("VAT") receivable	4,307	2,202
Receivable - other	2,499	1,884
Other	65	125
Total	$ 11,706	$ 9,130

Other Accrued Expenses

Other accrued expenses are comprised of the following (in thousands):

	December 31, 2021	December 31, 2020
Accrued personnel costs	$ 15,714	$ 18,334
Accrued interest payable for convertible senior notes	3,283	2,991
Income tax payable	1,579	907
Accrued corporate legal fees and professional services	141	459
Accrued royalties	5,463	6,617
Accrued variable considerations	17,211	11,701
Accrued legal settlement loss	2,325	—
Accrued expenses - other	5,155	4,199
Total	$ 50,871	$ 45,208

Segment Information

We have two operating and reportable segments, U.S. and ex-U.S., based on product revenue by geographic areas. We designated our reporting segments based on the internal reporting used by the Chief Operating Decision Maker ("CODM"), which is our Chief Executive Officer, for making decisions and assessing performance as the source of our reportable segments. The CODM allocates resources and assesses the performance of each operating segment based on product revenue by geographic areas. Accordingly, we view our business as two reportable operating segments to evaluate performance, allocate resources, set operational targets and forecast our future period financial results.

We manage our assets on a company basis, not by segments, as many of our assets are shared or commingled. Our CODM does not regularly review asset information by reportable segment. The majority of long-lived assets for both segments are located in the United States.

Research and Development Expense

Research and development costs are charged to expense as incurred and include, but are not limited to, salary and benefits, share-based compensation, clinical trial activities, drug development and manufacturing, companion diagnostic development and third-party service fees, including contract research organizations and investigative sites.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred and are reflected on the Consolidated Balance Sheets as prepaid or accrued research and development expenses.

Acquired In-Process Research and Development Expense

We have acquired and expect to continue to acquire the rights to develop and commercialize new drug candidates. The upfront payments to acquire a new drug compound, as well as subsequent milestone payments, are immediately expensed as acquired in-process research and development provided that the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no alternative future use. Once regulatory approval is received, payments to acquire rights, and the related milestone payments, are capitalized and the amortization of such assets recorded to product cost of sales.

Share-Based Compensation Expense

Share-based compensation is recognized as expense for all share-based awards made to employees and directors and is based on estimated fair values. We determine equity-based compensation at the grant date using the Black-Scholes option pricing model. The value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period. Any changes to the estimated forfeiture rates are accounted for prospectively.

Advertising Expense

In connection with the FDA approval and commercial launch of Rubraca in 2016, we began to incur advertising costs. Advertising costs are expensed when services are performed, or goods are delivered. We incurred $18.1 million, $17.0 million and $21.2 million in expense for the years ended December 31, 2021, 2020 and 2019, respectively.

Legal Settlement Loss

Following our regulatory announcement in November 2015 of adverse developments in our ongoing clinical trials for rociletinib, we and certain of our current and former executives were named in various securities lawsuits. As a result of these lawsuits, during the year ended December 31, 2021, we recorded a charge of $2.3 million to settle the Consolidated Derivative Complaint discussed in Note 12, *Commitments and Contingencies.* During 2019, we recorded a charge of $26.8 million to settle the Antipodean Complaint.

Concentration of Credit Risk

Financial instruments that potentially subject us to concentrations of credit risk are primarily cash and cash equivalents. We maintain our cash and cash equivalent balances in the form of money market accounts with financial institutions that we believe are creditworthy. We have no financial instruments with off-balance sheet risk of accounting loss.

Foreign Currency

The assets and liabilities of our foreign operations are translated into U.S. dollars at current exchange rates and the results of operations are translated at the average exchange rates for the reported periods. The resulting translation adjustments are included in accumulated other comprehensive loss on the Consolidated Balance Sheets. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. Transaction gains and losses are recorded to foreign currency gains (losses) on the Consolidated Statements of Operations and Comprehensive Loss. As of December 31, 2021, and 2020, approximately 4% and 3%, respectively, of our total liabilities were denominated in currencies other than the functional currency.

Income Taxes

We account for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Tax benefits are recognized when it is more likely than not that a tax position will be sustained during an audit. Deferred tax assets are reduced by a valuation allowance if current evidence indicates that it is considered more likely than not that these benefits will not be realized.

Recently Adopted Accounting Standards

In August 2020, the FASB issued guidance that simplifies an issuer’s accounting for debt and equity instruments. The guidance is effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. Early application is permitted. We adopted this guidance on January 1, 2022 and there was no material impact on our consolidated financial statements and related disclosures.

3. Revenue Recognition

We are currently approved to sell Rubraca in the United States and Europe markets. We distribute our product principally through a limited number of specialty distributor and specialty pharmacy providers, collectively, our customers. Our customers subsequently sell our products to patients and health care providers. We do not believe the loss of one of these customers would significantly impact the ability to distribute our product as we expect that sales volume would be absorbed evenly by the remaining customers. Separately, we have arrangements with certain payors and other third parties that provide for government-mandated and privately-negotiated rebates, chargebacks and discounts.

Product Revenue

Revenue from product sales are recognized when the performance obligation is satisfied, which is when customers obtain control of our product at a point in time, typically upon delivery. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from price concessions that include rebates, chargebacks, discounts, co-pay assistance, estimated product returns and other allowances that are offered within contracts between us and our customers, health care providers, payors and other indirect customers relating to the sales of our product. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable or a current liability. Where appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we adjust these estimates, which would affect product revenue and earnings in the period such variances become known.

Government Rebates. Rebates include mandated discounts under the Medicaid Drug Rebate Program, the Medicare coverage gap program, the Tricare health program and various European National Health Service, Sick Fund and Clawback programs. Rebates are amounts owed after the final dispensing of products to a benefit plan participant and are based upon contractual agreements or legal requirements with the public-sector benefit providers. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the Consolidated Balance Sheets. Our rebate estimates are based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. The accrual for rebates is based on the expected utilization from historical data we have accumulated since the Rubraca product launch.

GPO and Payor Rebates. We contract with various private payor organizations and group purchasing organizations ("GPO"), primarily insurance companies, pharmacy benefit managers and hospitals, for the payment of rebates with respect to utilization of our products. We estimate these rebates and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Chargebacks. Chargebacks are discounts that occur when contracted customers, which currently consist primarily of GPOs, Public Health Service ("PHS") organizations and federal government entities purchasing via the Federal Supply Schedule, purchase directly from our specialty distributors at a discounted price. The specialty distributor, in turn, charges back the difference between the price initially paid by the specialty distributor and the discounted price paid to the specialty distributor by the healthcare provider. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. The accrual for specialty distributor chargebacks is estimated based on known chargeback rates and known sales to specialty distributors adjusted for the estimated utilization by healthcare providers.

Discounts and Fees. Our payment terms range from 30 to 60 days. Specialty distributors and specialty pharmacies are offered various forms of consideration, including service fees and prompt pay discounts for payment within a specified period. We expect these customers will earn prompt pay discounts and therefore, we deduct the full amount of these discounts and service fees from product sales when revenue is recognized.

Co-pay assistance. Patients who have commercial insurance and meet certain eligibility requirements may receive co-pay assistance. The intent of this program is to reduce the patient's out of pocket costs. Liabilities for co-pay assistance are based on actual program participation provided by third-party administrators at month end.

Returns. Consistent with industry practice, we generally offer customers a right of return limited only to product that is considered short dated or product that is six months beyond the expiration date. To date, we have had minimal product returns and we currently do not have an accrual for product returns. We will continue to assess our estimate for product returns based on additional historical experience.

Product revenue from each of our customers who individually accounted for 10% or more of total revenues, which were all customers in the U.S. segment, consisted of the following:

	December 31, 2021	December 31, 2020
Customer A	15%	21%
Customer B	9%	14%
Customer C	15%	18%
Customer D	11%	11%
Customer E	5%	10%
Customer F	16%	6%

4. Property and Equipment

Property and equipment consisted of the following (in thousands):

	December 31,	
	2021	2020
Laboratory, manufacturing and office equipment	$ 1,145	$ 1,267
Leasehold improvements	12,111	17,256
Furniture and fixtures	2,735	2,782
Computer hardware and software	2,013	1,835
Total property and equipment	18,004	23,140
Less: accumulated depreciation	(11,450)	(11,055)
Total property and equipment, net	$ 6,554	$ 12,085

Depreciation expense related to property and equipment was approximately $3.1 million, $3.0 million and $3.0 million for the years ended December 31, 2021, 2020 and 2019, respectively.

5. Fair Value Measurements

Fair value is defined as the exchange price that would be received to sell an asset or paid to transfer a liability (at exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The three levels of inputs that may be used to measure fair value include:

Level 1: Quoted prices in active markets for identical assets or liabilities. Our Level 1 assets consist of money market investments. We do not have Level 1 liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities in active markets or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities. We do not have Level 2 assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity. We do not have Level 3 assets or liabilities.

The following table identifies our assets that were measured at fair value on a recurring basis (in thousands):

	Balance	Level 1	Level 2	Level 3
December 31, 2021				
Assets:				
Money market investments	$ 72,934	$ 72,934	$ —	$ —
Total assets at fair value	$ 72,934	$ 72,934	$ —	$ —
December 31, 2020				
Assets:				
Money market investments	$ 147,921	$ 147,921	$ —	$ —
Total assets at fair value	$ 147,921	$ 147,921	$ —	$ —

There were no liabilities that were measured at fair value on a recurring basis as of December 31, 2021 or 2020.

Financial instruments not recorded at fair value include our convertible senior notes. At December 31, 2021, the carrying amount of the 2024 Notes (2019 Issuance) was $84.4 million, which represents the aggregate principal amount net of remaining debt issuance costs, and the fair value was $65.1 million. At December 31, 2021, the carrying amount of the 2024 Notes (2020 Issuance) was $56.8 million, which represents the aggregate principal amount net of remaining debt issuance costs, and the fair value was $47.5 million. At December 31, 2021, the carrying amount of the 2025 Notes was $295.5 million, which represents the aggregate principal amount net of remaining debt issuance costs, and the fair value was $205.4 million. The fair value was determined using Level 2 inputs based on the indicative pricing published by certain investment banks or trading levels of the convertible senior notes, which are not listed on any securities exchange or quoted on an inter-dealer automated quotation system. See Note 9, *Debt* for discussion of the convertible senior notes. The carrying amounts of accounts payable and accrued expenses approximate their fair value due to their short-term maturities.

6. Inventories

The following table presents inventories as of December 31, 2021 and December 31, 2020 (in thousands):

	December 31, 2021	December 31, 2020
Work-in-process	$ 85,084	$ 102,507
Finished goods, net	38,452	32,330
Total inventories	$ 123,536	$ 134,837

At December 31, 2021, we had $13.7 million of current inventory and $109.8 million of long-term inventory.

7. Intangible Assets

At December 31, 2021 and 2020, intangible assets related to capitalized milestones under license agreements consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Intangible asset - milestones	$ 79,850	$ 79,850
Accumulated amortization	(19,479)	(14,107)
Total intangible asset, net	$ 60,371	$ 65,743

The estimated useful lives of these intangible assets are based on the estimated remaining patent life of Rubraca and extend through 2031 in Europe and 2035 in the U.S.

We recorded amortization expense of $5.4 million and $5.2 million related to capitalized milestone payments during the year ended December 31, 2021 and December 31, 2020, respectively. Amortization expense is included in cost of sales – intangible asset amortization on the Consolidated Statements of Operations and Comprehensive Loss.

Estimated future amortization expense for intangible assets as of December 31, 2021 is as follows (in thousands):

2022	$ 5,371
2023	5,371
2024	5,371
2025	5,371
2026	5,371
Thereafter	33,516
	$ 60,371

8. Leases

At the inception of an arrangement, we determine whether the arrangement is or contains a lease based on the unique facts and circumstances. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. We elected not to recognize on the balance sheet leases with terms of one year or less. Lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, we utilize the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term at an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

The components of a lease should be split into three categories: lease components (e.g. land, building, etc.), non-lease components (e.g. common area maintenance, maintenance, consumables, etc.) and non-components (e.g. property taxes, insurance, etc.). Then the fixed and in-substance fixed contract consideration (including any related to non-components) must be allocated based on fair values assigned to the lease components and non-lease components.

Our facilities operating leases have lease components, non-lease components and non-components, which we have separated because the non-lease components and non-components have variable lease payments and are excluded from the measurement of the lease liabilities. The lease component results in a right-of-use asset being recorded on the balance sheet and amortized as lease expense on a straight-line basis to the statements of operations.

We lease all of our office facilities in the U.S. and Europe. Leases with an initial term of 12 months or less are not recorded on the balance sheet; we recognize lease expense for these leases on a straight-line basis over the lease term. Most leases include one or more options to renew. The exercise of lease renewal options is at our sole discretion. Our lease agreements do not contain any material residual value guarantees or material restrictive covenants.

Prior to June 30, 2021, we had a finance lease and operating lease for certain equipment at the production train at Lonza, our non-exclusive manufacturer of the Rubraca API. Pursuant to the terms of Amendment 2 discussed in Note 12, *Commitments and Contingencies*, we derecognized the lease components recognized under the original agreement with Lonza. This includes the operating lease liabilities and right-of-use ("ROU") assets, finance lease liabilities and ROU assets and leasehold improvement assets and liability. The derecognition of the lease components, payment of $1.1 million to Lonza and derecognition of fixed assets related to our Lonza production train resulted in a loss of $0.3 million, which is included in other operating expenses on the Consolidated Statements of Operations and Comprehensive Loss for the year ended December 31, 2021. We also evaluated the prepaid manufacturing costs for impairment and determined that there was no impairment for the year ended December 31, 2021.

The components of lease expense and related cash flows were as follows (in thousands):

	Year ended December 31, 2021	Year ended December 31, 2020
Lease cost		
Finance lease cost:		
Amortization of right-of-use assets	$ 947	$ 1,895
Interest on lease liabilities	363	816
Operating lease cost	5,223	4,649
Short-term lease cost	320	401
Variable lease cost	2,193	2,071
Total lease cost	$ 9,046	$ 9,832
Operating cash flows from finance leases	$ 363	$ 816
Operating cash flows from operating leases	$ 5,223	$ 4,649
Financing cash flows from finance leases	$ 780	$ 1,470

The weighted-average remaining lease term and weighted-average discount rate were as follows:

	December 31, 2021	December 31, 2020
Weighted-average remaining lease term (years)		
Operating leases	5.9	6.6
Finance leases	N/A	5.0
Weighted-average discount rate		
Operating leases	8%	8%
Finance leases	N/A	8%

Future minimum commitments due under these lease agreements as of December 31, 2021 are as follows (in thousands):

	Operating Leases
2022	5,224
2023	4,673
2024	4,669
2025	4,825
2026	4,955
Thereafter	4,952
Present value adjustment	(6,153)
Present value of lease payments	$ 23,145

9. Debt

The following is a summary of our convertible senior notes at December 31, 2021 and 2020 (principal amount in thousands):

	Principal Amount December 31, 2021	Principal Amount December 31, 2020	Interest Rate	Maturity Date	Conversion rate per $1,000 principal amount (shares)
2021 Notes	$ —	$ 64,418	2.50%	September 15, 2021	16.1616
2024 Notes (2019 Issuance)	85,782	85,782	4.50%	August 1, 2024	137.2213
2024 Notes (2020 Issuance)	57,500	57,500	4.50%	August 1, 2024	160.3334
2025 Notes	300,000	300,000	1.25%	May 1, 2025	13.1278
Total	443,282	507,700			
Unamortized debt issuance costs	(6,510)	(8,656)			
Convertible senior notes	$ 436,772	$ 499,044			

2021 Notes

In September 2014, we completed a private placement of $287.5 million aggregate principal amount of 2.5% convertible senior notes due 2021 (the "2021 Notes") resulting in net proceeds of $278.3 million after deducting offering expenses. In accordance with the accounting guidance, the conversion feature did not meet the criteria for bifurcation, and the entire principal amount was recorded as a long-term liability on the Consolidated Balance Sheets.

In April 2020, we entered into a privately negotiated exchange agreement with a holder ("Holder") of our 2021 Notes, pursuant to which we issued to such Holder of the 2021 Notes approximately $36.1 million in aggregate principal amount of our currently outstanding 2024 Notes (2019 Issuance) in exchange for approximately $32.8 million in aggregate principal of 2021 Notes held by such Holder (the "Exchange Transaction"), which resulted in a $3.3 million loss on extinguishment of debt. We did not receive any cash proceeds from the Exchange Transaction.

On September 15, 2021, we paid off in full the $64.4 million in principal outstanding of our 2021 Notes.

2024 Notes (2019 Issuance)

In August 2019, we completed a private placement to qualified institutional buyers of $263.0 million aggregate principal amount of 4.50% convertible senior notes due 2024 (the "2024 Notes (2019 Issuance)") resulting in net proceeds of $254.9 million, after deducting underwriting discounts and commissions and offering expenses. In accordance with the accounting guidance, the conversion feature did not meet the criteria for bifurcation, and the entire principal amount was recorded as a long-term liability on the Consolidated Balance Sheets.

The 2024 Notes (2019 Issuance) are governed by the terms of the indenture between the Company, as issuer, and The Bank of New York Mellon Trust Company, N.A., as trustee. The 2024 Notes (2019 Issuance) are senior unsecured obligations and bear interest at a rate of 4.50% per year, payable semi-annually in arrears on February 1 and August 1 of each year. The 2024 Notes (2019 Issuance) will mature on August 1, 2024, unless earlier repurchased or converted.

Holders may convert all or any portion of the 2024 Notes (2019 Issuance) at any time prior to the close of business on the business day immediately preceding the maturity date. Upon conversion, the holders will receive shares of our common stock at an initial conversion rate of 137.2213 shares per $1,000 in principal amount of 2024 Notes (2019 Issuance), equivalent to a conversion price of approximately $7.29 per share. The conversion rate is subject to adjustment upon the occurrence of certain events described in the indenture. In addition, following certain corporate events that occur prior to the maturity date or upon our issuance of a notice of redemption, we will increase the conversion rate for holders who elect to convert the 2024 Notes (2019 Issuance) in connection with such a corporate event or during the related redemption period in certain circumstances.

We will not have the right to redeem the 2024 Notes (2019 Issuance) prior to their maturity. If we undergo a fundamental change, as defined in the indenture, prior to the maturity date of the 2024 Notes (2019 Issuance), holders may require us to repurchase for cash all or any portion of the 2024 Notes (2019 Issuance) at a fundamental change repurchase price equal to 100% of the principal amount of the 2024 Notes (2019 Issuance) to be repurchased plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. No sinking fund is provided for the 2024 Notes (2019 Issuance).

The 2024 Notes (2019 Issuance) rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the 2024 Notes (2019 Issuance); equal in right of payment to all of our liabilities that are not so subordinated, including the 2025 Notes; effectively junior in right of payment to any secured indebtedness to the extent of the value of the assets securing such indebtedness, including our borrowing under the Sixth Street financing agreement; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

In connection with the issuance of the 2024 Notes (2019 Issuance), we incurred $8.0 million of debt issuance costs. The debt issuance costs are presented as a deduction from the convertible senior notes on the Consolidated Balance Sheets and are amortized as interest expense over the expected life of the 2024 Notes (2019 Issuance) using the effective interest method. We determined the expected life of the debt was equal to the five-year term of the 2024 Notes (2019 Issuance).

In January 2020, we completed a registered direct offering of an aggregate 17,777,679 shares of our common stock at a price of $9.25 per share to a limited number of holders of our 2024 Notes (2019 Issuance). We used the proceeds of the share offering to repurchase from such holders an aggregate of $123.4 million principal amount of 2024 Notes (2019 Issue) in privately negotiated transactions. In addition, we paid customary fees and expenses in connection with the transactions. As a result, $3.6 million of unamortized debt issuance costs were derecognized and we recognized a $7.8 million loss on the transactions.

In April 2020, we completed the Exchange Transaction discussed in the 2021 Notes section above.

The additional 2024 Notes (2019 Issuance) issued in the Exchange Transaction were issued as additional notes under that certain Indenture, dated as of August 13, 2019 (the "Indenture"), by and between the Company and The Bank of New York Mellon Trust Company, N.A., as trustee, and have substantially identical terms to our currently outstanding 2024 Notes (2019 Issuance), except that the additional 2024 Notes (2019 Issuance) will accrue interest from February 1, 2020 and the initial interest payment date on the additional 2024 Notes (2019 Issuance) was August 1, 2020. The Holder paid to the Company accrued interest on the additional 2024 Notes (2019 Issue) from February 1, 2020 to and including April 20, 2020. The additional 2024 Notes (2019 Issuance) are treated as a single series of securities with the currently outstanding 2024 Notes (2019 Issuance).

In April and May 2020, approximately $24.3 million in principal amount of 2024 Notes (2019 Issuance) were converted into 3,331,870 shares of our common stock at the conversion rate of 137.2213 shares per $1,000 in principal amount of 2024 Notes (2019 Issuance).

In November 2020, we entered into a privately negotiated exchange and purchase agreement with a holder of our 2024 Notes (2019 Issuance). Pursuant to the agreement, in exchange for approximately $64.8 million aggregate principal amount of 2024 Notes (2019 Issuance) held by the holder, we agreed to issue to the holder a number shares of our common stock (the "Exchanged Shares") utilizing an exchange ratio that is based in part on the daily volume-weighted average prices ("VWAPs") per share of our common stock during a seven-day pricing period following execution of the agreement.

In addition, pursuant to the agreement, we sold to the holder $57.5 million aggregate principal amount of a new series of 4.50% Convertible Senior Notes due 2024 (the "2024 Notes (2020 Issuance)") at a purchase price of $1,000 per $1,000 principal amount thereof.

The number of Exchanged Shares was calculated utilizing an exchange ratio that is based in part on the average VWAPs of our common stock (subject to a floor) during a seven-day pricing period beginning on November 5, 2020 and ending on, and including, November 13, 2020. In November 2020, we issued 15,112,848 Exchanged Shares pursuant to the debt exchange transaction. As a result, $1.4 million of unamortized debt issuance costs were derecognized and we recognized a $27.3 million loss on the transactions.

2024 Notes (2020 Issuance)

The 2024 Notes (2020 Issuance) are governed by the terms of the indenture between the Company, as issuer, and The Bank of New York Mellon Trust Company, N.A., as trustee. The 2024 Notes (2020 Issuance) are senior unsecured obligations and bear interest at a rate of 4.50% per year, payable semi-annually in arrears on February 1 and August 1 of each year. The 2024 Notes (2020 Issuance) will mature on August 1, 2024, unless earlier repurchased or converted.

Holders may convert all or any portion of the 2024 Notes (2020 Issuance) at any time prior to the close of business on the business day immediately preceding the maturity date. Upon conversion, the holders will receive shares of our common stock at an initial conversion rate of 160.3334 shares per $1,000 in principal amount of 2024 Notes (2020 Issuance), equivalent to a conversion price of approximately $6.24 per share. The initial conversion price represents a premium of approximately 10% to the last reported sale price of $5.67 per share on November 4, 2020. The conversion rate is subject to adjustment upon the occurrence of certain events described in the indenture. In addition, following certain corporate events that occur prior to the maturity date or upon our issuance of a notice of redemption, we will increase the conversion rate for holders who elect to convert the 2024 Notes (2020 Issuance) in connection with such a corporate event or during the related redemption period in certain circumstances.

We will not have the right to redeem the 2024 Notes (2020 Issuance) prior to their maturity. If we undergo a fundamental change, as defined in the indenture, prior to the maturity date of the 2024 Notes (2020 Issuance), holders may require us to repurchase for cash all or any portion of the 2024 Notes (2020 Issuance) at a fundamental change repurchase price equal to 100% of the principal amount of the 2024 Notes (2020 Issuance) to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. No sinking fund is provided for the 2024 Notes (2020 Issuance).

The 2024 Notes (2020 Issuance) rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the 2024 Notes (2020 Issuance); equal in right of payment to all of our liabilities that are not so subordinated, including the 2024 Notes (2019 Issuance) and 2025 Notes; effectively junior in right of payment to any secured indebtedness to the extent of the value of the assets securing such indebtedness, including our borrowing under the Sixth Street financing agreement, as described subsequently herein; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

In connection with the issuance of the 2024 Notes (2020 Issuance), we incurred $0.9 million of debt issuance costs. The debt issuance costs are presented as a deduction from the convertible senior notes on the Consolidated Balance Sheets and are amortized as interest expense over the expected life of the 2024 Notes (2020 Issuance) using the effective interest method. We determined the expected life of the debt was equal to the four-year term of the 2024 Notes (2020 Issuance).

2025 Notes

In April 2018, we completed an underwritten public offering of $300.0 million aggregate principal amount of 1.25% convertible senior notes due 2025 (the "2025 Notes") resulting in net proceeds of $290.9 million, after deducting underwriting discounts and commissions and offering expenses. In accordance with the accounting guidance, the conversion feature did not meet the criteria for bifurcation, and the entire principal amount was recorded as a long-term liability on the Consolidated Balance Sheets.

The 2025 Notes are governed by the terms of the indenture between the Company, as issuer, and The Bank of New York Mellon Trust Company, N.A., as trustee, as supplemented by the terms of that certain first supplemental indenture thereto. The 2025 Notes are senior unsecured obligations and bear interest at a rate of 1.25% per year, payable semi-annually in arrears on May 1 and November 1 of each year. The 2025 Notes will mature on May 1, 2025, unless earlier converted, redeemed or repurchased.

Holders may convert all or any portion of the 2025 Notes at any time prior to the close of business on the business day immediately preceding the maturity date. Upon conversion, the holders will receive shares of our common stock at an initial conversion rate of 13.1278 shares per $1,000 in principal amount of 2025 Notes, equivalent to a conversion price of approximately $76.17 per share. The conversion rate is subject to adjustment upon the occurrence of certain events described in the indenture. In addition, following certain corporate events that occur prior to the maturity date or upon our issuance of a notice of redemption, we will increase the conversion rate for holders who elect to convert the 2025 Notes in connection with such a corporate event or during the related redemption period in certain circumstances.

On or after May 2, 2022, we may redeem the 2025 Notes, at our option, in whole or in part, if the last reported sale price of our common stock has been at least 150% of the conversion price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending not more than two trading days preceding the date on which we provide written notice of redemption at a redemption price equal to 100% of the

principal amount of the 2025 Notes to be redeemed plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the 2025 Notes.

If we undergo a fundamental change, as defined in the indenture, prior to the maturity date of the 2025 Notes, holders may require us to repurchase for cash all or any portion of the 2025 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2025 Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The 2025 Notes rank senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the 2025 Notes; effectively junior in right of payment to any secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

In connection with the issuance of the 2025 Notes, we incurred $9.1 million of debt issuance costs. The debt issuance costs are presented as a deduction from the convertible senior notes on the Consolidated Balance Sheets and are amortized as interest expense over the expected life of the 2025 Notes using the effective interest method. We determined the expected life of the debt was equal to the seven-year term of the 2025 Notes.

As of December 31, 2021, and 2020, the balance of unamortized debt issuance costs related to the convertible senior notes was $6.5 million and $8.7 million, respectively.

Maturities of our convertible notes consisted of the following as of December 31, 2021 (in thousands):

2022	$ —
2023	—
2024	143,282
2025	300,000
2026	—
Thereafter	—
	443,282
Less debt issuance costs	(6,510)
Current portion	—
Long-term portion	$ 436,772

Sixth Street Financing Agreement

On May 1, 2019, we entered into a financing agreement (the "Financing Agreement") with certain affiliates of Sixth Street Partners, LLC ("Sixth Street") in which we plan to borrow from Sixth Street amounts required to reimburse our actual costs and expenses incurred during each fiscal quarter (limited to agreed budgeted amounts), as such expenses are incurred, related to the ATHENA clinical trial, in an aggregate amount of up to $175 million (the amount actually borrowed, the "Borrowed Amount"). ATHENA is our largest clinical trial, with a target enrollment of 1,000 patients across more than 270 sites in at least 25 countries. The Clovis-sponsored phase 3 ATHENA study in advanced ovarian cancer is in the first-line maintenance treatment setting evaluating Rubraca plus nivolumab (PD-1 inhibitor), Rubraca, nivolumab and a placebo in newly-diagnosed patients who have completed platinum-based chemotherapy. This study initiated in the second quarter of 2018, completed enrollment during the second quarter of 2020, and top-line data readouts from the ATHENA study are anticipated in 2022, contingent upon the occurrence of the protocol-specified PFS events.

We incur borrowings under the Financing Agreement on a quarterly basis, beginning with such expenses incurred during the quarter ended March 31, 2019 and ending generally on the earliest to occur of (i) the termination of the ATHENA Trial, (ii) the date of completion of all activities under the ATHENA Trial Clinical Study Protocol, (iii) the date on which we pay the Discharge Amount (as defined in the Financing Agreement), (iv) the date of the occurrence of a change of control of us (or a sale of all or substantially all of our assets related to Rubraca) or our receipt of notice of certain breaches by us of our obligations under material in-license agreements related to Rubraca and (v) September 30, 2022.

We are obligated to repay on a quarterly basis, 30 days after the end of the quarter, beginning on the earliest to occur of (i) the termination of the ATHENA Trial, (ii) the approval by the FDA of an update to the label portion of the Rubraca new drug application ("NDA") to include in such label the treatment of an indication resulting from the ATHENA Trial, (iii) the date on which we determine that the results of the ATHENA Trial are insufficient to achieve such an expansion of the Rubraca label to cover an indication based on the ATHENA Trial and (iv) September 30, 2022 (the "Repayment Start Date"). We expect to make the first payment by October 30, 2022, unless one of the other events occurs prior to September 30, 2022.

- 9.75% (which rate may be increased incrementally up to approximately 10.25% in the event the Borrowed Amount exceeds $166.5 million) of the direct Rubraca net sales recorded by us and our subsidiaries worldwide and our future out-licensees in the United States, if any, during such quarter;

- 19.5% of any royalty payments received by us and our subsidiaries during such quarter based on the sales of Rubraca by our future out-licensees outside the United States, if any; and

- 19.5% of any other amounts received by us and our subsidiaries in connection with any other commercialization arrangement for Rubraca, including any upfront and milestone payments and proceeds of infringement claims (which payments are not subject to the caps described below).

Quarterly payments are capped at $8.5 million, unless the label portion of the Rubraca NDA is expanded by the FDA to include on such label the treatment of an indication resulting from the ATHENA Trial, in which case the quarterly payment is capped at $13.5 million. In the event the aggregate Borrowed Amount exceeds $166.5 million, such quarterly limits will be incrementally increased to a maximum of approximately $8.94 million and $14.19 million, respectively. The maximum amount required to be repaid under the agreement is two times the aggregate Borrowed Amount, which may be $350 million in the event we borrow the full $175 million under the Financing Agreement.

In the event we have not made payments on or before December 30, 2025 equal to at least the Borrowed Amount, we are required to make a lump sum payment in an amount equal to such Borrowed Amount less the aggregate of all prior quarterly payments described above. All other payments are contingent on the performance of Rubraca. There is no final maturity date on the Financing Agreement.

Our obligations under the Financing Agreement are secured under a Pledge and Security agreement by a first priority security interest in all of our assets related to Rubraca, including intellectual property rights and a pledge of the equity of our wholly owned subsidiaries, Clovis Oncology UK Limited and Clovis Oncology Ireland Limited. In addition, the obligations are guaranteed by Clovis Oncology UK Limited and Clovis Oncology Ireland Limited, secured by a first priority security interest in all the assets of those subsidiaries.

Pursuant to the Financing Agreement, we have agreed to certain limitations on our operations, including limitations on making certain restricted junior payments, including payment of dividends, limitation on liens and certain limitations on the ability of our non-guarantor subsidiaries to own certain assets related to Rubraca and to incur indebtedness.

We may terminate the Financing Agreement at any time by paying the lenders an amount (the "Discharge Amount") equal to the sum of (a) (A) (i) if such date is prior to the Repayment Start Date, 1.75 times the Borrowed Amount or (ii) if such date is after the Repayment Start Date, 2.00 times the Borrowed Amount minus (B) the aggregate amount of all quarterly payments previously paid to the lenders plus (b) all other obligations which have accrued but which have not been paid under the loan documents, including expense reimbursement.

In the event of (i) a change of control of us, we must pay the Discharge Amount to the lenders and (ii) an event of default under the Financing Agreement (which includes, among other events, breaches or defaults under or terminations of our material in-license agreements related to Rubraca and defaults under our other material indebtedness), the lenders have the right to declare the Discharge Amount to be immediately due and payable.

For the year ended December 31, 2021, we recorded $170.0 million as a long-term liability on the Consolidated Balance Sheets and future quarterly draws will be recorded as a long-term liability on the Consolidated Balance Sheets. In connection with the transaction, we incurred $1.8 million of debt issuance costs. The debt issuance costs are presented as a deduction from the Sixth Street financing liability on the Consolidated Balance Sheets and are amortized as interest

expense over the expected life of the Financing Agreement using the straight-line method. As of December 31, 2021, and 2020 the balance of unamortized debt issuance costs was $1.3 million and $1.5 million, respectively.

For the year ended December 31, 2021, we used an effective interest rate of 13.7%. For subsequent periods, we will use the prospective method whereby a new effective interest rate is determined based on the revised estimate of remaining cash flows. The new rate is the discount rate that equates the present value of the revised estimate of remaining cash flows with the carrying amount of the debt, and it will be used to recognize interest expense for the remaining periods. Under this method, the effective interest rate is not constant, and any change in expected cash flows is recognized prospectively as an adjustment to the effective yield.

Amounts reflected on the balance sheet and in the table below in respect of the Financing Agreement represent the maximum amounts payable by us to the lenders during the periods indicated. Payments due under our Financing Agreement are based, for the most part, on net sales of Rubraca by us and our licensees. Rubraca sales have not been consistent historically and sales in future periods are difficult to predict. Therefore, expected maturities of our Financing Agreement as of December 31, 2021 (in thousands) are shown below based on the quarterly capped amount described above and certain other mandatory payments set forth in the Financing Agreement. Actual payments may fluctuate and may be less than the amounts reflected in the table below. See above for a full description of the Financing Agreement and our payment obligations thereunder.

2022	$ 8,500
2023	34,000
2024	34,000
2025	70,718
2026	34,000
Thereafter	113,218
	294,436
Less debt issuance costs	(1,278)
Less unrecognized interest	(114,702)
Current portion	(8,500)
Long-term portion	$ 169,956

The following table sets forth total interest expense recognized during the years ended December 31, 2021, 2020 and 2019 (in thousands):

	Year ended December 31,		
	2021	2020	2019
Interest on convertible notes	$ 11,363	$ 11,934	$ 13,680
Amortization of debt issuance costs	2,430	2,672	2,858
Debt issuance cost derecognized related to convertible debt transactions	—	4,345	—
Interest on finance lease	363	816	759
Interest on borrowings under financing agreement	19,894	10,624	1,997
Other interest	53	117	111
Total interest expense	$ 34,103	$ 30,508	$ 19,405

10. Stockholders' Equity

Common Stock

The holders of common stock are entitled to one vote per share on all matters to be voted upon by our stockholders. Subject to the preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends, if any, as may be declared by our board of directors.

In May 2020, we sold 11,090,000 shares of our common stock in a public offering at $8.05 per share. The net proceeds from the offering were $82.8 million, after deducting underwriting discounts and commissions and offering expenses.

On May 17, 2021, we entered into a distribution agreement (the "Distribution Agreement") with J.P. Morgan Securities LLC and BofA Securities, Inc., as agents (the "Agents"), pursuant to which we may offer and sell, from time to time, through the Agents, shares of our common stock having an aggregate offering price of up to $75.0 million in transactions that are deemed to be "at the market" offerings as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, including sales made by means of ordinary brokers' transactions, including directly on the Nasdaq Global Select Market or into any other existing trading market for the Shares, or sales made to or through a market maker, in block transactions or by any other method permitted by law, including negotiated transactions. Sales may be made at market prices prevailing at the time of a sale or at prices related to prevailing market prices or at negotiated prices. During the period between May 18, 2021 and June 9, 2021, we sold an aggregate of 13,492,231 shares of our common stock under the Distribution Agreement resulting gross proceeds of $75.0 million and net proceeds to us of $72.5 million, after deducting commissions and offering expenses, effectively closing out sales we may make pursuant to the Distribution Agreement. We have used and intend to use the net proceeds of this offering for general corporate purposes, including funding of our development programs, sales and marketing expenses associated with Rubraca, repayment, repurchase or refinance of our debt obligations, payment of milestones pursuant to our license agreements, general and administrative expenses, acquisition or licensing of additional product candidates or businesses and working capital.

On August 16, 2021, we entered into a distribution agreement (the "August Distribution Agreement") with the Agents, pursuant to which we may offer and sell, from time to time, through the Agents, shares of our common stock, having an aggregate offering price of up to $125.0 million in transactions that are deemed to be "at the market" offerings as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, including sales made by means of ordinary brokers' transactions, including directly on the Nasdaq Global Select Market or into any other existing trading market for the shares, or sales made to or through a market maker, in block transactions or by any other method permitted by law, including privately negotiated transactions. Sales may be made at market prices prevailing at the time of a sale or at prices related to prevailing market prices or at negotiated prices. During the period between August 17, 2021 and September 15, 2021, we sold an aggregate of 9,379,976 shares of our common stock under the August Distribution Agreement resulting in gross proceeds of $43.0 million and net proceeds to us of $41.5 million, after deducting commissions and offering expenses. During the period between November 5, 2021 and November 16, 2021, we sold an aggregate of 731,292 shares of our common stock resulting in gross proceeds of $3.1 million and net proceeds to us of $3.0 million, after deducting commissions and offering expenses.

Subsequent to year end, during the period between January 18, 2022 and February 15, 2022, we sold an aggregate of 12,967,044 shares of our common stock resulting in gross proceeds of $28.1 million and net proceeds to us of $27.2 million, after deducting commissions and offering expenses.

We have used and intend to use the net proceeds of this offering for general corporate purposes, including funding of our development programs, sales and marketing expenses associated with Rubraca, repayment, repurchase or refinance of our debt obligations, payment of milestones pursuant to our license agreements, general and administrative expenses, acquisition or licensing of additional product candidates or businesses and working capital.

Accumulated Other Comprehensive Loss

Accumulated other comprehensive loss consists of changes in foreign currency translation adjustments, which includes changes in a subsidiary's functional currency, and unrealized gains and losses on available-for-sale securities.

The changes in accumulated balances related to each component of other comprehensive income (loss) are summarized as follows (in thousands):

	Foreign Currency Translation Adjustments	Unrealized (Losses) Gains	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2019	$ (44,732)	$ (133)	$ (44,865)
Other comprehensive income (loss)	567	(6)	561
Total before tax	(44,165)	(139)	(44,304)
Tax effect	—	—	—
Balance at December 31, 2020	(44,165)	(139)	(44,304)
Other comprehensive income (loss)	874	—	874
Total before tax	(43,291)	(139)	(43,430)
Tax effect	—	—	—
Balance at December 31, 2021	$ (43,291)	$ (139)	$ (43,430)

There were no reclassifications out of accumulated other comprehensive loss in the years ended December 31, 2021, 2020 and 2019.

11. Share-Based Compensation

Stock Options

In April 2020, our board of directors approved the 2020 Stock Incentive Plan (the "2020 Plan"), which became effective upon approval. The 2020 Plan provides for the grant of nonqualified stock options, stock appreciation rights, restricted stock, restricted stock units, performance awards and other share-based awards to our employees and directors (collectively, "awards"). Common shares authorized for issuance under the 2020 Plan were 10,970,000 at December 31, 2021, which represents the initial reserve. Stock options granted vest ratably over either a one-year period or three-year period for Board of Director grants. Employee stock options generally vest over a three- or four-year period with 33% or 25%, respectively, of the options cliff-vesting after year one and the remaining options vesting ratably over each subsequent month. All stock options expire 10 years from the date of grant.

In August 2011, our board of directors approved the 2011 Stock Incentive Plan (the "2011 Plan"), which became effective upon the closing of our initial public offering in November 2011. The 2011 Plan provides for the granting of incentive and nonqualified stock options, stock appreciation rights, restricted stock, restricted stock units, performance awards and other share-based awards to our employees and directors. Stock options granted vest ratably over either a one-year period or three-year period for Board of Director grants. Employee stock options generally vest over a four-year period with 25% of the options cliff-vesting after year one and the remaining options vesting ratably over each subsequent month. All stock options expire 10 years from the date of grant.

The adoption of the 2020 Plan did not affect the terms and conditions of any outstanding awards granted under the 2011 Plan. Upon the adoption of the 2020 Plan, no future grants will be granted under the 2011 Plan, but the 2011 Plan will remain in effect with respect to outstanding awards granted thereunder.

Share-based compensation expense for the years ended December 31, 2021, 2020 and 2019, respectively, was recognized in the accompanying Consolidated Statements of Operations and Comprehensive Loss as follows (in thousands):

	Year ended December 31,		
	2021	2020	2019
Research and development	$ 12,924	$ 25,577	$ 25,838
Selling, general and administrative	12,529	25,217	28,466
Total share-based compensation expense	$ 25,453	$ 50,794	$ 54,304

We did not recognize a tax benefit related to share-based compensation expense during the years ended December 31, 2021, 2020 and 2019 as we maintain net operating loss carryforwards and have established a valuation allowance against the entire net deferred tax asset as of December 31, 2021.

The following table summarizes the activity relating to our options to purchase common stock:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (Thousands)
Outstanding at December 31, 2020	6,502,169	$ 37.78		
Granted	1,205,469	5.93		
Exercised	(7,087)	4.98		
Forfeited	(690,512)	27.41		
Outstanding at December 31, 2021	7,010,039	$ 33.36	5.4	$ —
Vested and expected to vest at December 31, 2021	6,868,290	$ 33.90	5.3	$ —
Vested and exercisable at December 31, 2021	5,518,597	$ 39.99	4.5	$ —

The aggregate intrinsic value in the table above represents the pretax intrinsic value, based on our closing stock price of $2.71 as of December 31, 2021, which would have been received by the option holders had all option holders with in-the-money options exercised their options as of that date.

The following table summarizes information about our stock options as of and for the years ended December 31, 2021, 2020 and 2019 (in thousands, except weighted-average grant date fair value per share):

	Year ended December 31,		
	2021	2020	2019
Weighted-average grant date fair value per share	$ 4.70	$ 5.67	$ 13.53
Intrinsic value of options exercised	$ 15	$ 381	$ 1,525
Cash received from stock option exercises	$ 35	$ 236	$ 1,361

As of December 31, 2021, the unrecognized share-based compensation expense related to unvested options, adjusted for expected forfeitures, was $8.4 million and the estimated weighted-average remaining vesting period was 1.5 years.

The fair value of each share-based award is estimated on the grant date using the Black-Scholes option pricing model based upon the weighted-average assumptions provided in the following table:

	Year ended December 31,		
	2021	2020	2019
Dividend yield	—	—	—
Volatility (a)	101 %	99 %	93 %
Risk-free interest rate (b)	1.30 %	0.49 %	1.67 %
Expected term (years) (c)	6.2	6.0	5.9

(a) *Volatility*: The expected volatility was estimated using our historical data.
(b) *Risk-free interest rate:* The rate is based on the yield on the grant date of a zero-coupon U.S. Treasury bond whose maturity period approximates the option's expected term.
(c) *Expected term:* The expected term of the award was estimated using our historical data.

The total fair value of stock options vested during the years ended December 31, 2021, 2020 and 2019 was $13.4 million, $22.4 million and $32.8 million, respectively.

Restricted Stock

Beginning in 2016, we issued restricted stock units ("RSUs") to our employees under the 2011 Plan and 2020 Plan. The RSUs vest either (i) over two years, with 50% vesting one year from the date of grant and the remaining 50% vesting two years from the date of grant or (ii) over four years, with 25% vesting one year from the date of grant and the remaining 75% vesting ratably each subsequent quarter over the following three years, as defined in the grant agreement. Vested RSUs are payable in shares of our common stock at the end of the vesting period. RSUs are measured based on the fair value of the underlying stock on the grant date. The minimum statutory tax on the value of common stock shares issued to employees upon vesting are paid by us through the sale of registered shares of our common stock.

The following table summarizes the activity related to our unvested RSUs:

	Number of Units	Weighted Average Grant Date Fair Value
Unvested at December 31, 2020	2,964,297	$ 14.36
Granted	2,689,091	6.19
Vested	(1,424,695)	16.76
Forfeited	(545,271)	8.30
Unvested at December 31, 2021	3,683,422	$ 8.36
Expected to vest after December 31, 2021	3,289,585	$ 8.51

As of December 31, 2021, the unrecognized share-based compensation expense related to RSUs, adjusted for expected forfeitures, was $25.9 million and the estimated weighted-average remaining vesting period was 1.9 years.

Common Stock Reserved for Issuance

As of December 31, 2021, we reserved shares of common stock for future issuance as follows:

	Common Stock Outstanding	Available for Grant or Future Issuance	Total Shares of Common Stock Reserved
2011 Stock Incentive Plan	6,783,310	—	6,783,310
2020 Stock Incentive Plan	3,910,151	7,049,071	10,959,222
2011 Employee Stock Purchase Plan	—	2,783,229	2,783,229
Total	10,693,461	9,832,300	20,525,761

Employee Stock Purchase Plan

In April 2021, our board of directors adopted and our shareholders subsequently approved in June 2021 the Clovis Oncology, Inc. 2021 Employee Stock Purchase Plan ("ESPP"). Under the 2021 ESPP, 3,000,000 shares of common stock are available for purchase. We adopted the 2021 ESPP because the 2011 ESPP expired pursuant to its terms on August 24, 2021. Upon approval of the 2021 ESPP, no future offerings were offered under the 2011 ESPP, but the 2011 ESPP will remain in effect with respect to current offerings thereunder.

The 2021 ESPP provides for consecutive six-month offering periods, during which participating employees may elect to have up to 10% of their compensation withheld and applied to the purchase of common stock at the end of each offering period. The purchase price of the common stock is 85% of the lower of the fair value of a share of common stock on the first trading date of each offering period or the fair value of a share of common stock on the last trading day of the offering period. The board of directors may amend the 2021 ESPP at any time in any respect they deem necessary or advisable, subject to shareholder approval for certain events. The board of directors or compensation committee may also suspend or terminate the 2021 ESPP at any time.

Under the 2011 ESPP, we sold 158,382 and 283,588 shares to employees in 2021 and 2020, respectively. Under the 2021 ESPP, we sold 216,771 shares to employees in 2021. There were 2,783,229 shares available for sale under the 2021 ESPP as of December 31, 2021. The weighted-average estimated grant date fair value of purchase awards under the 2011 ESPP and 2021 ESPP during the years ended December 31, 2021 and 2020 was $2.18 and $4.63 per share, respectively. The total share-based compensation expense recorded as a result of the 2011 ESPP and 2021 ESPP was approximately $0.7 million, $1.1 million and $1.0 million during the years ended December 31, 2021, 2020 and 2019, respectively. On February 9, 2022, the Compensation Committee of our Board of Directors amended the ESPP to reduce the total number of shares issuable thereunder from 3,000,000 to 1,000,000 shares.

The fair value of purchase awards issued to our employees during the years ended December 31, 2021, 2020 and 2019 was estimated using the Black-Scholes option pricing model based upon the weighted-average assumptions provided in the following table:

	Year ended December 31,		
	2021	2020	2019
Dividend yield	—	—	—
Volatility (a)	91 %	138 %	79 %
Risk-free interest rate (b)	0.10 %	0.90 %	2.20 %
Expected term (years) (c)	0.5	0.5	0.5

(a) *Volatility*: The expected volatility was estimated using our historical data.
(b) *Risk-free interest rate:* The rate is based on the U.S. Treasury yield in effect at the time of grant with terms similar to the contractual term of the purchase right.
(c) *Expected term:* The expected life of the award represents the six-month offering period for the Purchase Plan.

12. Commitments and Contingencies

Manufacture and Services Agreement Commitments

On October 3, 2016, we entered into a Manufacturing and Services Agreement (the "Agreement") with a non-exclusive third-party supplier for the production of the active ingredient for Rubraca. Under the terms of the Agreement, we will provide the third-party supplier a rolling forecast for the supply of the active ingredient in Rubraca that will be updated by us on a quarterly basis. We are obligated to order material sufficient to satisfy an initial quantity specified in a forecast. In addition, the third-party supplier has constructed, in its existing facility, a production train that will manufacture the Rubraca active ingredient. We made scheduled capital program fee payments toward capital equipment and other costs associated with the construction of the production train. Beginning in the fourth quarter of 2018, once the facility was operational, we were obligated to pay a fixed facility fee each quarter for the duration of the Agreement, which expires on December 31, 2025, unless extended by mutual consent of the parties. As of December 31, 2021, $43.4 million of purchase commitments remain under the Agreement.

At the time we entered into the Agreement, we evaluated the Agreement as a whole and bifurcated into lease and non-lease components, which consisted of an operating lease of warehouse space, financial lease of equipment, purchase of leasehold improvements and prepaid manufacturing costs based upon the relative fair values of each of the deliverables. During October 2018, the production train was placed into service and we recorded the various components of the Agreement.

On June 16, 2021, we entered into amendment no. 2 to the Agreement with Lonza ("Amendment 2"). Pursuant to the terms of Amendment 2, we paid Lonza $1.1 million to repurpose the production train so that Lonza will be able to use the facility to manufacture other products for third parties in addition to API for Clovis. Lonza is guaranteeing a minimum percentage usage of this production train for third parties and Lonza would reduce our fixed facility fee starting in 2023 based on this minimum percentage usage. If Lonza is able to utilize greater than the minimum guaranteed percentage, it will increase the reduction to our fixed facility fee. We evaluated Amendment 2 and determined that we no longer have a lease with Lonza at June 30, 2021 because Amendment 2 modified the terms of the Agreement in that Lonza will use a portion of the production train for third parties. The Agreement no longer conveys the right to direct the use of the identified asset and Clovis no longer has the right to obtain substantially all the economic benefit from the asset. As a result, the arrangement is no longer in scope of ASC 842, "Leases", resulting in the derecognition of the lease components recognized under the original agreement. This includes the operating lease liabilities and ROU assets, finance lease liabilities and ROU assets and leasehold improvement assets and liability. The derecognition of the lease components, payment of $1.1 million to Lonza and derecognition of fixed assets related to our Lonza production train resulted in a loss of $0.3 million, which is included in other operating expenses on the Consolidated Statements of Operations and Comprehensive Loss for the year ended December 31, 2021. We also evaluated the prepaid manufacturing costs for impairment and determined that there was no impairment for the year ended December 31, 2021.

Legal Proceedings

We and certain of our officers were named as defendants in several lawsuits, as described below. We cannot reasonably predict the outcome of these legal proceedings, nor can we estimate the amount of loss or range of loss, if any, that may result. An adverse outcome in these proceedings could have a material adverse effect on our results of operations, cash flows or financial condition.

Rociletinib-Related Litigation

In March 2017, two putative shareholders of the Company, Macalinao and McKenry ("Plaintiffs"), filed shareholder derivative complaints against certain directors and officers of the Company in the Court of Chancery of the State of Delaware. On May 4, 2017, the Macalinao and McKenry actions were consolidated for all purposes in a single proceeding under the caption In re Clovis Oncology, Inc. Derivative Litigation, Case No. 2017-0222 (the "Consolidated Derivative Action").

On May 18, 2017, Plaintiffs filed a Consolidated Verified Shareholder Derivative Complaint (the "Consolidated Derivative Complaint"). The Consolidated Derivative Complaint generally alleged that the defendants breached their fiduciary duties owed to the Company by allegedly causing or allowing misrepresentations of the Company's business operations and prospects, failing to ensure that the TIGER-X clinical trial for rociletinib was being conducted in accordance with applicable rules, regulations and protocols, and engaging in insider trading. The Consolidated Derivative Complaint sought, among other things, an award of money damages.

On July 31, 2017, the defendants filed a motion to dismiss the Consolidated Derivative Complaint. Plaintiffs filed an opposition to the motion to dismiss on August 31, 2017, and the defendants filed a reply in further support of the motion to dismiss on September 26, 2017.

While the motion to dismiss remained pending, on November 19, 2018, Plaintiffs filed a motion for leave to file a supplemental consolidated complaint, and on November 20, 2018, the Court granted that motion. On November 27, 2018, Plaintiffs filed their supplemental complaint (the "Supplemental Derivative Complaint"), which adds allegations concerning the Company's, Mr. Mahaffy's and Mr. Mast's settlements with the United States Securities and Exchange Commission. Pursuant to a briefing schedule entered by the Court, the defendants filed a supplemental motion to dismiss the Supplemental Derivative Complaint on February 6, 2019; Plaintiffs filed an opposition brief on February 22, 2019; and the defendants filed a reply brief on March 5, 2019. The Court held oral arguments on the defendants' motions to dismiss on June 19, 2019. At the oral arguments, the Court ordered the parties to submit supplemental letter briefs on the motion to dismiss.

On October 1, 2019, Vice Chancellor Joseph R. Slights III of the Delaware Chancery Court, issued a Memorandum Opinion granting in part and denying in part defendants' motions to dismiss. The Supplemental Derivative Complaint was dismissed as to Plaintiffs' derivative claims for unjust enrichment and insider trading. The Court allowed Plaintiffs' remaining derivative claim for breach of fiduciary duty to proceed. Defendants filed an answer to the Supplemental Derivative Complaint on December 27, 2019.

On December 17, 2019, the parties participated in a mediation, which did not result in a settlement. On December 22, 2019, the Company's Board of Directors formed a Special Litigation Committee (the "SLC") to conduct an investigation of the claims asserted in the Supplemental Derivative Complaint. On February 18, 2020, the SLC moved to stay all proceedings in the Consolidated Derivative Action pending completion of its investigation. Plaintiffs filed their opposition to the motion to stay on March 3, 2020 and the SLC filed its reply on March 13, 2020. On May 12, 2020, after hearing oral argument, Vice Chancellor Slights granted the SLC's motion to stay proceedings until September 18, 2020 so that the SLC may complete its investigation. On September 11, 2020, Vice Chancellor Slights granted the parties' request to extend the stay until October 31, 2020, to allow the SLC further time to complete its investigation. On October 26, 2020, Vice Chancellor Slights granted the parties' request to further extend the stay until November 15, 2020. On November 13, 2020, Vice Chancellor Slights granted the parties' request to further extend the stay until December 15, 2020.

On December 16, 2020, the SLC filed a report (the "SLC Report") containing the findings of its investigation. The SLC Report concludes that the claims asserted in the Consolidated Derivative Action lack merit. Specifically, the SLC Report finds that the defendants did not breach their fiduciary duties in connection with the Company's TIGER-X

clinical trial. Accordingly, on the same date that the SLC Report was filed, the SLC filed a motion to terminate the Consolidated Derivative Action in Delaware Chancery Court. A briefing schedule on the motion to terminate has not yet been set.

On March 26, 2021, in response to discovery requests from Plaintiffs, the SLC filed a motion for a protective order seeking to preclude discovery into the merits of the claims investigated by the SLC. On March 29, 2021, the Company joined the SLC's motion for a protective order. Pursuant to a scheduling stipulation entered by the Court on April 5, 2021, Plaintiffs filed an opposition to the motion for a protective order on April 16, 2021, and the SLC filed its reply on April 30, 2021. On August 10, 2021, Vice Chancellor Slights granted the parties' request to cancel oral argument on the SLC's motion for a protective order, pursuant to the parties' representation that they had reached an agreement on that motion.

On January 7, 2022, the Plaintiffs, the Company and the SLC participated in a mediation, which resulted in the parties reaching an agreement in principle to settle the pending litigation. Subject to the execution of a definitive settlement agreement and, among other conditions, court approval, the Company agreed to adopt certain corporate governance reforms, including, among other things, the election of one new independent director to the Clovis Board of Directors by the 2023 Annual Meeting of Stockholders and the creation of a management-level Disclosure Committee. Neither the Company nor any of the defendants would make a financial contribution towards the principal terms of the settlement. Moreover, under the terms of the agreement in principle, the Company agreed not to oppose or object to Plaintiffs' application for an award of attorneys' fees and expenses not to exceed $2.325 million in the aggregate, which amount as ultimately awarded by the Court would be payable by the Company.

European Patent Opposition

Two European patents in the rucaparib camsylate salt/polymorph patent family (European Patent 2534153 and its divisional European Patent 3150610) were opposed. In particular, opposition notices against European Patent 2534153 were filed by two parties on June 20, 2017. During an oral hearing that took place on December 4, 2018, the European Patent Office's Opposition Division maintained European Patent 2534153 in amended and narrowed form with claims to certain crystalline forms of rucaparib camsylate, including, but not limited to, rucaparib S-camsylate Form A, the crystalline form in Rubraca. Clovis and one opponent, Hexal AG, appealed the written decision of the European Opposition Division and filed reply appeal briefs in November 2019. An oral hearing in the appeal is scheduled on December 8, 2022.

An opposition against European Patent 3150610 was filed by Generics (UK) Limited on April 30, 2020 on grounds similar to those raised in the opposition notices against European Patent 2534153, which grounds are common in such proceedings. Clovis responded to the opposition notice in European Patent 3150610 by amending the claims to be directed to the use of rucaparib maleate in a method of inhibiting PARP activity or treating cancer. That is, the amended claims do not cover Rubraca. During an oral hearing that took place on November 18, 2021, European Patent 3150610 was revoked and the written decision of the European Patent Office was dated December 15, 2021. Clovis filed a notice of appeal on January 28, 2022 and intends to file an appeal brief before April 25, 2022. During the appeal, the effect of the Opposition Division's decision is suspended, and the patent remains in force until a Technical Board of Appeals issues its own decision.

In Europe, regulatory exclusivity is available for ten years, plus one year for a new indication; therefore, we have regulatory exclusivity for Rubraca, including all forms of rucaparib, in Europe until 2028, and if the EMA approves a subsequent indication that brings significant clinical benefit in comparison with existing therapies, until 2029.

13. License Agreements

Rubraca

In June 2011, we entered into a license agreement with Pfizer to obtain the exclusive global rights to develop and commercialize Rubraca. The exclusive rights are exclusive even as to Pfizer and include the right to grant sublicenses. Pursuant to the terms of the license agreement, we made a $7.0 million upfront payment to Pfizer and are required to make additional payments to Pfizer for the achievement of certain development and regulatory and sales milestones and royalties on sales as required by the license agreement. Prior to the FDA approval of Rubraca, we made milestone payments of $1.4 million, which were recognized as acquired in-process research and development expense.

During 2016 through 2020, we paid Pfizer a total of $82.5 million in milestone payments related to FDA and European Commission approvals received for Rubraca. These milestone payments were recognized as intangible assets and are amortized over the estimated remaining useful life of Rubraca.

We are obligated under the license agreement to use commercially reasonable efforts to develop and commercialize Rubraca and we are responsible for all ongoing development and commercialization costs for Rubraca. We are required to make regulatory milestone payments to Pfizer of up to an additional $8.0 million in aggregate if specified clinical study objectives and regulatory filings, acceptances and approvals are achieved. In addition, we are obligated to make sales milestone payments to Pfizer if specified annual sales targets for Rubraca are met, which relate to annual sales targets of $250.0 million and above, which, in the aggregate, could amount to total milestone payments of $170.0 million, and tiered royalty payments at a mid-teen percentage rate on net sales, with standard provisions for royalty offsets to the extent we need to obtain any rights from third parties to commercialize Rubraca.

The license agreement with Pfizer will remain in effect until the expiration of all of our royalty and sublicense revenue obligations to Pfizer, determined on a product-by-product and country-by-country basis, unless we elect to terminate the license agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, Pfizer can terminate the agreement, resulting in a loss of our rights to Rubraca and an obligation to assign or license to Pfizer any intellectual property rights or other rights we may have in Rubraca, including our regulatory filings, regulatory approvals, patents and trademarks for Rubraca.

In April 2012, we entered into a license agreement with AstraZeneca to acquire exclusive rights associated with Rubraca under a family of patents and patent applications that claim methods of treating patients with PARP inhibitors in certain indications. The license enables the development and commercialization of Rubraca for the uses claimed by these patents. AstraZeneca also receives royalties on net sales of Rubraca.

FAP-2286 and the Radionuclide Therapy Development Program

In September 2019, we entered into a global license and collaboration agreement with 3BP to develop and commercialize a PTRT and imaging agent targeting FAP. The lead candidate, designated internally as FAP-2286, is being developed pursuant to a global development plan agreed to by the parties. We are responsible for the costs of all preclinical and clinical development activities described in the plan, including the costs for a limited number of 3BP full-time equivalents and external costs incurred during the preclinical development phase of the collaboration. Upon the signing of the license and collaboration agreement in September 2019, we made a $9.4 million upfront payment to 3BP, which we recognized as acquired in-process research and development expense.

Pursuant to the terms of the FAP agreement, we are required to make additional payments to 3BP for annual technology access fees and upon the achievement of certain development and regulatory milestone events (or on certain dates, whichever occur earlier). We are also obligated to pay 3BP single- to low-double-digit royalties on net sales of the FAP-targeted therapeutic product and imaging agent, based on the volume of annual net sales achieved. In addition, 3BP is entitled to receive 34% of any consideration, excluding royalties on the therapeutic product, pursuant to any sublicenses we may grant.

We are obligated under the license and collaboration agreement to use diligent efforts to develop FAP-2286 and commercialize a FAP-targeted therapeutic product and imaging agent, and we are responsible for all commercialization costs in our territory. The agreement with 3BP will remain in effect until the expiration of our royalty obligations to 3BP, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement

earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, 3BP can terminate the agreement, resulting in a loss of our rights. 3BP also has the right to terminate the agreement under certain circumstances in connection with our change of control in which the acquiring party retains a product competitive with the FAP-targeted therapeutic product or, in the event marketing authorization has not yet been obtained, does not agree to the then-current global development plan.

We submitted two INDs for FAP-2286 for use as imaging and treatment agents in December 2020 to support an initial phase 1 study to determine the dose and tolerability of FAP-2286 as a therapeutic agent with expansion cohorts planned in multiple tumor types as part of a global development program. In April 2021, we made a milestone payment to 3BP under the license and collaboration agreement of $2.2 million as a result of the FDA's acceptance of the IND for the treatment agent. In September 2021, we made a $3.3 million milestone payment to 3BP under the license and collaboration agreement.

In February 2020, we finalized the terms of a drug discovery collaboration agreement with 3BP to identify up to three additional, undisclosed targets for PTRT, to which we will obtain global rights for any resulting product candidates. We are responsible for the costs of all preclinical and clinical development activities conducted under the discovery program, including the costs for a limited number of 3BP full-time equivalents and external costs incurred during the discovery and preclinical development phase for each collaboration target. The discovery collaboration agreement was effective December 31, 2019, for which we incurred a $2.1 million technology access fee, which we accrued and recognized as a research and development expense.

Pursuant to the terms of the discovery collaboration agreement, we are required to make additional payments to 3BP for annual technology access fees and upon the achievement of certain development and regulatory milestone events (or on certain dates, whichever occur earlier). We are also obligated to pay 3BP a 6% royalty on net sales of License Products (as defined in the agreement), based on the volume of quarterly net sales achieved.

We are obligated under the discovery collaboration agreement to use diligent efforts to develop and commercialize the product candidates, if any, that result from the discovery program, and we are responsible for all clinical development and commercialization costs. The agreement with 3BP will remain in effect until the expiration of our royalty obligations to 3BP, determined on a product-by-product and country-by-country basis, unless we elect to terminate the agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, 3BP can terminate the agreement, resulting in a loss of our rights.

Lucitanib

On November 19, 2013, we acquired all of the issued and outstanding capital stock of EOS pursuant to the terms set forth in that certain Stock Purchase Agreement, dated as of November 19, 2013 (the "Stock Purchase Agreement"), by and among the Company, EOS, its shareholders (the "Sellers") and Sofinnova Capital V FCPR, acting in its capacity as the Sellers' representative. Following the acquisition, EOS became a wholly-owned subsidiary of the Company. Under the terms of the Stock Purchase Agreement, in addition to the initial purchase price paid at the time of the closing of the acquisition and other license fees due to Advenchen described below, we will also be obligated to pay to the Sellers a milestone payment of $65.0 million upon obtaining the first NDA approval from the FDA with respect to lucitanib.

In October 2008, Ethical Oncology Science, S.p.A. ("EOS") (now known as Clovis Oncology Italy Srl) entered into an exclusive license agreement with Advenchen Laboratories LLC ("Advenchen") to develop and commercialize lucitanib on a global basis, excluding China.

We are obligated to pay Advenchen tiered royalties at percentage rates in the mid-single digits on net sales of lucitanib, based on the volume of annual net sales achieved. In addition, after giving effect to the first and second amendments to the license agreement, we are required to pay to Advenchen 25% of any consideration, excluding royalties, we receive from sublicensees, in lieu of the milestone obligations set forth in the agreement. We are obligated under the agreement to use commercially reasonable efforts to develop and commercialize at least one product containing lucitanib, and we are also responsible for all remaining development and commercialization costs for lucitanib.

The license agreement with Advenchen will remain in effect until the expiration of all of our royalty obligations to Advenchen, determined on a product-by-product and country-by-country basis, unless we elect to terminate the

agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, Advenchen can terminate the agreement, resulting in a loss of our rights to lucitanib.

14. Net Loss Per Common Share

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed by dividing net loss by the weighted-average number of common share equivalents outstanding using the treasury-stock method for the stock options and RSUs and the if-converted method for the convertible senior notes. As a result of our net losses for the periods presented, all potentially dilutive common share equivalents were considered anti-dilutive and were excluded from the computation of diluted net loss per share.

The shares outstanding at the end of the respective periods presented in the table below were excluded from the calculation of diluted net loss per share due to their anti-dilutive effect (in thousands):

	Year ended December 31,		
	2021	2020	2019
Common shares under stock incentive plans	3,683	3,095	2,480
Convertible senior notes	24,928	25,969	41,598
Total potential dilutive shares	28,611	29,064	44,078

15. Income Taxes

We are subject to U.S. federal, state and foreign income tax. The geographical components of loss before income taxes consisted of the following (in thousands):

	Year ended December 31,		
	2021	2020	2019
Domestic	$ (265,578)	$ (370,839)	$ (399,497)
Foreign	650	1,080	871
Total loss before income taxes	$ (264,928)	$ (369,759)	$ (398,626)

The income tax provision consists of the following current and deferred tax expense (benefit) amounts (in thousands):

	Year ended December 31,		
	2021	2020	2019
Current tax:			
U.S. Federal & State	$ 18	$ 50	$ 3
Foreign	(422)	(597)	1,795
Total current expense (benefit)	(404)	(547)	1,798
Deferred tax:			
U.S. Federal & State	—	—	—
Foreign	—	—	—
Total deferred (benefit)	—	—	—
Total income tax expense (benefit)	$ (404)	$ (547)	$ 1,798

A reconciliation of the U.S. federal statutory income tax rate to our effective tax rate is provided below:

	Year ended December 31,		
	2021	2020	2019
Federal income tax benefit at statutory rate	21.0 %	21.0 %	21.0 %
State income tax benefit, net of federal benefit	2.6	1.6	2.9
Tax credits	2.3	1.5	1.1
Change in uncertain tax positions	(0.2)	(0.1)	4.3
Convertible debt transactions	—	(2.2)	—
Prior year true ups	1.1	(0.9)	(0.1)
Share based compensation	(2.5)	(2.6)	(2.3)
Tax rate changes	2.4	(1.4)	(0.1)
Change in valuation allowance	(25.4)	(16.1)	(26.5)
Other	(1.1)	(0.6)	(0.8)
Effective income tax rate	0.2 %	0.2 %	(0.5)%

The significant components of our deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforward	$ 441,548	$ 414,932
Tax credit carryforwards	250,781	247,064
Interest expense limitation carryforward	8,026	5,371
Intangible assets	125,679	94,558
Share-based compensation expense	31,246	33,169
Product acquisition costs	5,571	4,992
Lease liabilities	5,553	6,122
Accrued liabilities and other	10,253	7,488
Total deferred tax assets	878,657	813,696
Valuation allowance	(873,898)	(806,622)
Deferred tax assets, net of valuation allowance	4,759	7,074
Deferred tax liabilities:		
Right-of-use assets	(4,581)	(6,799)
Prepaid expenses and fixed assets	(178)	(275)
Total deferred tax liabilities	(4,759)	(7,074)
Net deferred tax liability	$ —	$ —

The Tax Cuts and Jobs Act (the "Act"), enacted in the U.S. on December 22, 2017, subjects a U.S. shareholder to tax on the Global Intangible Low-Taxed Income ("GILTI") earned by certain foreign subsidiaries. The FASB Staff Q&A, Topic 740, No. 5, "Accounting for Global Intangible Low-Taxed Income", states that an entity can make an accounting policy election to either recognize deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. We have elected to account for GILTI in the year the tax is incurred.

The realization of deferred tax assets is dependent upon a number of factors including future earnings, the timing and amount of which is uncertain. A valuation allowance was established for the net deferred tax asset balance due to management's belief that the realization of these assets is not likely to occur in the foreseeable future. We recorded a net increase to the valuation allowance of $67.3 million and $56.1 million for the years ended December 31, 2021 and 2020, respectively, primarily due to the growth in net operating losses and amortizable research and development expenses incurred during the year.

In addition, we recognize tax benefits if it is more likely than not to be sustained under audit by the relevant taxing authority based on technical merits. An uncertain tax position will not be recognized if it has less than a 50% likelihood of being sustained during audit. If the threshold is met, the tax benefit is measured and recognized at the largest amount above the greater than 50% likelihood threshold at time of settlement. The balance of unrecognized tax benefits at December 31, 2021 of $8.5 million, if recognized, would not impact our effective tax rate as long as we remain subject

to a full valuation allowance. The following table summarizes the gross amounts of unrecognized tax benefits (in thousands):

	Year ended December 31,	
	2021	2020
Balance at beginning of year	$ 8,004	$ 7,525
Changes related to prior period tax positions	31	64
Additions related to current period tax positions	450	415
Settlements with tax authorities	—	—
Expiration of statute of limitations	—	—
Balance at end of year	$ 8,485	$ 8,004

As of December 31, 2021, we had approximately $1.8 billion, $1.7 billion and zero of U.S. federal, state and foreign net operating loss carryforwards, respectively. The U.S. federal net operating losses, generated prior to the enactment of the Act, totaling $1.1 billion, will expire from 2029 to 2037 if not utilized and the U.S. federal net operating losses generated after the enactment of the Act, totaling $0.7 billion, do not expire and are carried forward indefinitely. U.S. state net operating losses will expire from 2025 to 2041 if not utilized. We have research and development and orphan drug tax credit carryforwards of $259.3 million that will expire from 2030 through 2041 if not utilized.

We believe that a change in ownership as defined under Section 382 of the U.S. Internal Revenue Code occurred as a result of our public offering of common stock completed in April 2012. Future utilization of the federal net operating losses ("NOL") and tax credit carryforwards accumulated from inception to the change in ownership date will be subject to annual limitations to offset future taxable income. It is possible that a change in ownership will occur in the future, which will limit the NOL amounts generated since the last estimated change of ownership. Our federal and state income taxes for the period from January 1, 2009 to December 31, 2014, other than the orphan drug tax credit, and January 1, 2016 through December 31, 2021 remain open to an audit. Our foreign subsidiaries are also subject to tax audits by tax authorities in the jurisdictions where they operate for the periods from December 31, 2017 to December 31, 2021.

We may be assessed interest and penalties related to the settlement of tax positions and such amounts will be recognized within income tax expense when assessed. To date, no interest and penalties have been recognized.

16. Employee Benefit Plans

We maintain a retirement plan, which is qualified under section 401(k) of the Internal Revenue Code for our U.S. employees. The plan allows eligible employees to defer, at the employee's discretion, pretax compensation up to the IRS annual limits. We matched contributions up to 4% of the eligible employee's compensation or the maximum amount permitted by law. Total expense for contributions made to U.S. employees was approximately $1.9 million, $2.1 million and $2.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. Our international employees participate in retirement plans or postretirement life insurance plans governed by the local laws in effect for the country in which they reside. We made contributions to the retirement plans or postretirement life insurance plans of international employees of approximately $1.4 million, $1.5 million and $1.1 million for the years ended December 31, 2021, 2020 and 2019, respectively.

17. Segment Information

The following table presents information about our reportable segments for the year months ended December 31, 2021, 2020 and 2019 (in thousands):

	Year ended December 31,								
	2021			2020			2019		
	U.S.	Ex-U.S.	Total	U.S.	Ex-U.S.	Total	U.S.	Ex-U.S.	Total
Product revenue	$ 115,673	$ 33,084	$ 148,757	$ 146,259	$ 18,263	$ 164,522	$ 137,187	$ 5,819	$ 143,006
Operating expenses:									
Cost of sales - product	22,526	10,929	33,455	29,526	6,602	36,128	28,179	1,747	29,926
Cost of sales - intangible asset amortization	2,480	2,891	5,371	2,287	2,890	5,177	1,956	2,804	4,760
Research and development	178,643	7,959	186,602	249,444	8,263	257,707	275,518	7,628	283,146
Selling, general and administrative	104,145	24,255	128,400	139,455	24,439	163,894	161,132	21,637	182,769
Acquired in-process research and development	5,476	—	5,476	—	—	—	9,440	—	9,440
Other operating expenses	15,220	—	15,220	3,804	—	3,804	9,711	—	9,711
Total expenses	328,490	46,034	374,524	424,516	42,194	466,710	485,936	33,816	519,752
Operating loss	$ (212,817)	$ (12,950)	(225,767)	$ (278,257)	$ (23,931)	(302,188)	$ (348,749)	$ (27,997)	(376,746)
Other income (expense):									
Interest expense			(34,103)			(30,508)			(19,405)
Foreign currency loss			(3,177)			(72)			(547)
Loss on convertible senior notes conversion			—			(35,075)			—
(Loss) gain on extinguishment of debt			—			(3,277)			18,480
Legal settlement loss			(2,325)			—			(26,750)
Other income			444			1,361			6,342
Other income (expense), net			(39,161)			(67,571)			(21,880)
Loss before income taxes			(264,928)			(369,759)			(398,626)
Income tax (expense) benefit			404			547			(1,798)
Net loss			$ (264,524)			$ (369,212)			$ (400,424)

18. Quarterly Information (Unaudited)

The results of operations on a quarterly basis for the years ended December 31, 2021 and 2020 were as follows (in thousands):

	March 31, 2021	June 30, 2021	September 30, 2021	December 31, 2021	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
Revenues:								
Product revenue	$ 38,053	$ 36,820	$ 37,916	$ 35,968	$ 42,564	$ 39,887	$ 38,772	$ 43,299
Operating expenses:								
Cost of sales - product	8,268	8,294	8,506	8,387	9,096	9,120	8,438	9,474
Cost of sales - intangible asset amortization	1,343	1,343	1,343	1,342	1,212	1,280	1,343	1,342
Research and development	52,805	45,759	46,222	41,816	68,221	69,878	62,902	56,706
Selling, general and administrative	29,941	32,918	32,196	33,345	42,598	41,902	38,636	40,758
Acquired in-process research and development	—	2,204	3,272	—	—	—	—	—
Other operating expenses	3,707	3,884	3,841	3,788	3,449	355	—	—
Total expenses	96,064	94,402	95,380	88,678	124,576	122,535	111,319	108,280
Operating loss	(58,011)	(57,582)	(57,464)	(52,710)	(82,012)	(82,648)	(72,547)	(64,981)
Other income (expense):								
Interest expense	(8,037)	(8,770)	(8,786)	(8,510)	(9,561)	(6,739)	(6,859)	(7,349)
Foreign currency (loss) gain	(546)	(206)	(1,248)	(1,177)	(877)	142	633	30
Loss on convertible senior notes conversion	—	—	—	—	(7,791)	—	—	(27,284)
Loss on extinguishment of debt	—	—	—	—	—	(3,277)	—	—
Legal settlement loss	—	—	—	(2,325)	—	—	—	—
Other income	183	107	101	53	841	239	79	202
Other income (expense), net	(8,400)	(8,869)	(9,933)	(11,959)	(17,388)	(9,635)	(6,147)	(34,401)
Loss before income taxes	(66,411)	(66,451)	(67,397)	(64,669)	(99,400)	(92,283)	(78,694)	(99,382)
Income tax benefit (expense)	134	3	(13)	280	68	36	18	425
Net loss	$ (66,277)	$ (66,448)	$ (67,410)	$ (64,389)	$ (99,332)	$ (92,247)	$ (78,676)	$ (98,957)
Basic and diluted net loss per common share	$ (0.64)	$ (0.61)	$ (0.56)	$ (0.50)	$ (1.39)	$ (1.15)	$ (0.89)	$ (1.02)
Basic and diluted weighted average common shares outstanding	102,246	108,481	121,217	128,471	71,662	80,453	88,255	96,681

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CLOVIS ONCOLOGY, INC.

By: /S/ PATRICK J. MAHAFFY
Patrick J. Mahaffy
President and Chief Executive Officer; Director

Date: February 23, 2022

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Name	Title	Date
/S/ PATRICK J. MAHAFFY **Patrick J. Mahaffy**	President and Chief Executive Officer; Director *(Principal Executive Officer)*	February 23, 2022
/S/ DANIEL W. MUEHL **Daniel W. Muehl**	Executive Vice President and Chief Finance Officer *(Principal Financial Officer and Principal Accounting Officer)*	February 23, 2022
/S/ BRIAN G. ATWOOD **Brian G. Atwood**	Director	February 23, 2022
/S/ ROBERT W. AZELBY **Robert W. Azelby**	Director	February 23, 2022
/S/ JAMES C. BLAIR **James C. Blair**	Director	February 23, 2022
/S/ RICHARD A. FAIR **Richard A. Fair**	Director	February 23, 2022
/S/ KEITH FLAHERTY **Keith Flaherty**	Director	February 23, 2022
/S/ GINGER L. GRAHAM **Ginger L. Graham**	Director	February 23, 2022
/S/ PAUL KLINGENSTEIN **Paul Klingenstein**	Director	February 23, 2022
/S/ EDWARD J. MCKINLEY **Edward J. McKinley**	Director	February 23, 2022
/S/ RONIT SIMANTOV **Ronit Simantov**	Director	February 23, 2022
/S/ THORLEF SPICKSCHEN **Thorlef Spickschen**	Director	February 23, 2022

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-253485) of Clovis Oncology, Inc.,

(2) Registration Statement (Form S-8 No. 333-257168) pertaining to the Clovis Oncology, Inc. Amended and Restated 2020 Stock Incentive Plan and the Clovis Oncology, Inc. 2021 Employee Stock Purchase Plan,

(3) Registration Statement (Form S-8 No. 333-238936) pertaining to the Clovis Oncology, Inc. 2020 Stock Incentive Plan and Clovis Oncology, Inc. 2011 Employee Stock Purchase Plan,

(4) Registration Statements (Form S-8 Nos. 333-234600, 333-226523, 333-211948, 333-206193, 333-198022, 333-190565) pertaining to the Clovis Oncology, Inc. 2011 Stock Incentive Plan Amended and Restated,

(5) Registration Statements (Form S-8 Nos. 333-219046 and 333-182278) pertaining to the Clovis Oncology, Inc. 2011 Stock Incentive Plan Amended and Restated and Clovis Oncology 2011 Employee Stock Purchase Plan, and

(6) Registration Statement (Form S-8 No. 333-178283) pertaining to the Clovis Oncology, Inc. 2011 Stock Incentive Plan Amended and Restated, Clovis Oncology, Inc. 2011 Employee Stock Purchase Plan and Clovis Oncology, Inc. 2009 Equity Incentive Plan;

of our reports dated February 23, 2022, with respect to the consolidated financial statements of Clovis Oncology, Inc., and the effectiveness of internal control over financial reporting of Clovis Oncology, Inc., included in this Annual Report (Form 10-K) of Clovis Oncology, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Denver, Colorado
February 23, 2022

Exhibit 31.1

I, Patrick J. Mahaffy, certify that:

1. I have reviewed this annual report on Form 10-K of Clovis Oncology, Inc. for the year ended December 31, 2021;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 23, 2022

/s/ PATRICK J. MAHAFFY

Patrick J. Mahaffy
President and Chief Executive Officer

Exhibit 31.2

I, Daniel W. Muehl, certify that:

1. I have reviewed this annual report on Form 10-K of Clovis Oncology, Inc. for the year ended December 31, 2021;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 23, 2022

/s/ DANIEL W. MUEHL

Daniel W. Muehl
Executive Vice President and Chief Financial Officer

Exhibit 32.1

CERTIFICATIONS PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002
(18 U.S.C. SECTION 1350)

In connection with the Annual Report of Clovis Oncology, Inc., a Delaware corporation (the "Company"), on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the "Report"), Patrick J. Mahaffy, as President and Chief Executive Officer of the Company, does hereby certify, pursuant to §906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. §1350), that to his knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 23, 2022

/s/ PATRICK J. MAHAFFY
Patrick J. Mahaffy
President and Chief Executive Officer

Exhibit 32.2

CERTIFICATIONS PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002
(18 U.S.C. SECTION 1350)

In connection with the Annual Report of Clovis Oncology, Inc., a Delaware corporation (the "Company"), on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the "Report"), Daniel W. Muehl, as Executive Vice President and Chief Finance Officer of the Company, does hereby certify, pursuant to §906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. §1350), that to his knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 23, 2022

/s/ DANIEL W. MUEHL
Daniel W. Muehl
Executive Vice President and Chief Finance Officer