UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2021

OR

☐ **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 001-34655

AVEO PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3581650**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**

30 Winter Street, Boston, Massachusetts 02108
(Address of principal executive offices) (Zip Code)

(857) 400-0101
(Registrant's telephone number, including area code)

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, $0.001 par value	AVEO	Nasdaq Capital Market

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" and "smaller reporting 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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Number of shares of the registrant's Common Stock, $0.001 par value, outstanding on May 7, 2021: 34,360,775.

AVEO PHARMACEUTICALS, INC.

FORM 10-Q
FOR THE QUARTER ENDED MARCH 31, 2021

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Cautionary Note Regarding Forward-Looking Statements and Industry Data

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. All statements other than statements of historical fact contained in this report are statements that could be deemed forward-looking statements, including, without limitation, statements with respect to the plans, strategies and objectives of management for future operations; statements concerning product research, development and commercialization plans, timelines and anticipated results; statements of expectation or belief; statements with respect to clinical trials and studies; statements with respect to the therapeutic potential of product candidates; any expectations of revenue, expenses, earnings or losses from operations, or other financial results; and statements of assumptions underlying any of the foregoing. Without limiting the foregoing, the words “anticipates”, “believes”, “could”, “estimates”, “expects”, “intends”, “may”, “plans”, “seeks”, “will”, “strategy”, “potential”, “should”, “would” and other similar language, whether in the negative or affirmative, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements may include, but are not limited to, statements about:

- our plans to launch and commercialize FOTIVDA;
- our plans to develop our clinical stage assets and commercialize our product candidates;
- our manufacturing, marketing and sales capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our products;
- the initiation, timing, progress and results of future clinical trials, and our development programs;
- our ability to secure new collaborations, maintain existing collaborations or obtain additional funding;
- our intellectual property position;
- the potential of ficlatuzumab, AV-380 or other product candidates that we in-license, or may elect to in-license, or may acquire in the future;
- the timing or likelihood of regulatory filings and approvals;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our competitive position;
- developments and projections relating to our competitors and our industry;
- impacts resulting from the COVID-19 pandemic and responsive actions relating thereto;
- our estimates of the period in which we anticipate that existing cash, cash equivalents and investments will enable us to fund our current and planned operations; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors. We therefore caution you against relying on any of these forward-looking statements. Important factors that could cause actual results to differ materially from those in these forward-looking statements include the factors discussed below under the heading “Risk Factor Summary,” and the risk factors detailed further in Item 1A., “Risk Factors” of Part I of this report and in our U.S. Securities and Exchange Commission reports filed after this report.

This report also includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this report involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

The forward-looking statements included in this quarterly report represent our estimates as of the filing date of this quarterly report. We specifically disclaim any obligation to update these forward-looking statements in the future. These forward-looking statements should not be relied upon as representing our estimates or views as of any date subsequent to the date of this annual report.

Risk Factor Summary

Investment in our securities involves risk. You should carefully consider the following summary of what we believe to be the principle risks facing our business, in addition to the risks described more fully in Item 1A., "Risk Factors" of Part I of this Quarterly Report on Form 10-Q and other information included in this report. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations.

If any of the following risks occur, our business, financial condition and results of operations and future growth prospects could be materially and adversely affected, and the actual outcomes of matters as to which forward-looking statements are made in this report could be materially different from those anticipated in such forward-looking statements.

- We have incurred significant operating losses, anticipate that we will continue to incur significant operating expenses for the foreseeable future and may never generate significant revenue or achieve or sustain profitability.
- We may require substantial additional funding to advance our pipeline of clinical stage assets, and if we are unable to obtain this necessary capital when needed, we could be forced to delay, limit, reduce or terminate our research, product development or commercialization efforts.
- We have only recently transitioned from a development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We depend heavily on the success of our product, FOTIVDA, and on our clinical stage assets, including tivozanib (in other indications), ficlatuzumab and AV-380. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize our product candidates, our business will be materially harmed.
- If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, receipt of necessary regulatory approvals could be delayed or prevented.
- If clinical trials of any product candidates that we, or any collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.
- We face substantial competition from existing approved products and our competitors may also discover, develop or commercialize new competing products before, or more successfully, than we do.
- Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.
- We rely in part on third parties to produce our preclinical and clinical product candidate supplies and to conduct clinical trials of our internally-developed product candidates, and those third parties may not perform satisfactorily, including by failing to deliver supplies on time or to meet deadlines for the completion of such trials, research or testing.
- We rely on our licensee EUSA, over whom we have little control, for the sales, marketing and distribution efforts associated with the commercialization of FOTIVDA in certain European countries and any failure by EUSA to devote the necessary resources and attention to market and sell FOTIVDA effectively and successfully may materially impact our ability to generate revenue.
- We may not be successful in establishing or maintaining strategic partnerships to further the development of our therapeutic programs. Additionally, if any of our current or future strategic partners fails to perform its obligations or terminates the partnership, the development and commercialization of the product candidates under such agreement could be delayed or terminated and, such failures or terminations could have a material adverse effect on our operations and business.
- We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our product candidates, or the scope of our patent protection could be insufficiently broad, which could result in competition and a decrease in the potential market share for our product candidates.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
(In thousands, except par value amounts)
(Unaudited)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 121,414	$ 61,761
Marketable securities	—	—
Trade receivables, net	1,144	1,197
Partnership receivables	1,422	—
Clinical trial retainers	587	355
Other prepaid expenses and other current assets	1,495	2,195
Total current assets	126,062	65,508
Property and equipment, net	326	343
Operating lease right-of-use asset	790	903
Other assets	258	158
Total assets	$ 127,436	$ 66,912
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,963	$ 3,380
Accrued clinical trial costs and contract research	5,285	4,550
Other accrued liabilities	4,723	4,463
Operating lease liability	331	369
Loans payable, net of discount	—	1,056
Deferred revenue	1,974	1,974
Deferred research and development reimbursements	112	164
PIPE Warrant liability (Note 7)	2,595	199
Other liabilities (Note 6)	790	790
Total current liabilities	19,773	16,945
Loans payable, net of current portion and discount	32,437	12,716
Deferred revenue, non-current	85	578
Operating lease liability, non-current	261	336
Other liabilities, non-current (Note 6)	2,432	1,043
Total liabilities	54,988	31,618
Stockholders' equity:		
Preferred stock, $.001 par value: 5,000 shares authorized at March 31, 2021 and December 31, 2020; no shares issued and outstanding at each of March 31, 2021 and December 31, 2020	—	—
Common stock, $.001 par value: 50,000 shares authorized at March 31, 2021 and December 31, 2020; 34,361 shares issued and outstanding at March 31, 2021 and 26,883 issued and outstanding at December 31, 2020	34	27
Additional paid-in capital	715,741	656,472
Accumulated deficit	(643,327)	(621,205)
Total stockholders' equity	72,448	35,294
Total liabilities and stockholders' equity	$ 127,436	$ 66,912

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations
(In thousands, except per share amounts)
(Unaudited)

	Three Months Ended March 31,	
	2021	**2020**
Revenues:		
FOTIVDA product revenue, net	$ 1,066	$ -
Collaboration and licensing revenue	493	493
Partnership royalties	361	291
	1,920	784
Operating expenses:		
Cost of products sold	138	-
Research and development	5,797	7,826
Selling, general and administrative	15,100	3,672
	21,035	11,498
Loss from operations	(19,115)	(10,714)
Other income (expense), net:		
Interest expense, net	(611)	(315)
Change in fair value of PIPE Warrant liability	(2,396)	2,648
Other income (expense), net	(3,007)	2,333
Net loss	$ (22,122)	$ (8,381)
Net loss per share - basic and diluted	$ (0.81)	$ (0.52)
Weighted average number of common shares outstanding	27,429	16,081

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Income (Loss)
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2021	**2020**
Net loss	$ (22,122)	$ (8,381)
Other comprehensive income (loss):		
Unrealized gain (loss) on available-for-sale securities	—	—
Comprehensive loss	$ (22,122)	$ (8,381)

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(In thousands)
(Unaudited)

	Common Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value				
Balance at December 31, 2020	26,883	$ 27	$ 656,472	$ —	$ (621,205)	$ 35,294
Issuance of common stock in a public offering (net of issuance costs of $3.6 million)	6,900	7	51,596	—	—	51,603
Issuance of common stock from the SVB Leerink sales agreement (net of issuance costs of $0.1 million)	331	—	3,377	—	—	3,377
Issuance of common stock in connection with warrant exercises	247	—	3,092	—	—	3,092
Stock-based compensation expense related to equity- classified awards	—	—	1,204	—	—	1,204
Net loss	—	—	—	—	(22,122)	(22,122)
Balance at March 31, 2021	34,361	$ 34	$ 715,741	$ —	$ (643,327)	$ 72,448

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(In thousands)
(Unaudited)

	Common Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value				
Balance at December 31, 2019	16,081	$ 16	$ 600,451	$ —	$ (585,621)	$ 14,846
Stock-based compensation expense related to equity- classified awards	—	—	543	—	—	543
Net loss	—	—	—	—	(8,381)	(8,381)
Balance at March 31, 2020	16,081	$ 16	$ 600,994	$ —	$ (594,002)	$ 7,008

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2021	2020
Operating activities		
Net loss	$ (22,122)	$ (8,381)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	17	—
Stock-based compensation	1,204	543
Non-cash interest expense	140	109
Non-cash change in fair value of PIPE Warrant liability	2,396	(2,648)
Amortization of premium and discount on investments	—	(51)
Changes in operating assets and liabilities:		
Trade receivables, net	(1,144)	(1,148)
Partnership receivables	(225)	—
Prepaid expenses and other current assets	468	559
Operating lease right-of-use asset	113	(1,383)
Other non-current assets	(100)	—
Accounts payable	583	1,499
Accrued contract research	735	(580)
Other accrued liabilities	260	(860)
Operating lease liability	(38)	438
Deferred revenue	(493)	(493)
Deferred research and development reimbursements	(52)	117
Operating lease liability, non-current	(76)	592
Net cash used in operating activities	(18,334)	(11,687)
Investing activities		
Purchases of marketable securities	—	(7,152)
Proceeds from maturities and sales of marketable securities	—	15,000
Purchases of property and equipment	—	(100)
Net cash provided by investing activities	—	7,748
Financing activities		
Proceeds from issuance of common stock, net of issuance costs	54,980	—
Proceeds from issuance of loan payable	20,000	—
Proceeds from warrant exercises	3,092	—
Payment on principal of loan payable (Note 6)	—	(2,389)
Payment of debt issuance costs	(85)	—
Net cash provided by (used in) financing activities	77,987	(2,389)
Net increase (decrease) in cash and cash equivalents	59,653	(6,328)
Cash and cash equivalents at beginning of period	61,761	29,785
Cash and cash equivalents at end of period	$ 121,414	$ 23,457
Supplemental cash flow information		
Cash paid for interest	$ 362	$ 368
Right-of-use asset obtained in exchange for operating lease liabilities	$ —	$ 1,225

See accompanying notes.

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. The Company's strategy is to focus its resources on the development and commercialization of its product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. With the approval of its first commercial product, FOTIVDA® (tivozanib), in the United States, the Company has transitioned from a clinical development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company.

FOTIVDA is the Company's lead product and was approved by the U.S. Food and Drug Administration ("FDA"), for marketing and sale in the United States on March 10, 2021. FOTIVDA is approved in the United States for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma following two or more prior systemic therapies. FOTIVDA is an oral, next-generation vascular endothelial growth factor receptor ("VEGFR") tyrosine kinase inhibitor ("TKI"). The FDA approval of FOTIVDA is based on the Company's pivotal phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, Nexavar® (sorafenib), in renal cell carcinoma ("RCC") patients whose disease had relapsed or become refractory to two or three prior systemic therapies, which the Company refers to as the TIVO-3 trial. The approval is also supported by three additional trials in RCC and includes safety data from over 1,000 clinical trial subjects. FOTIVDA became commercially available in the United States on March 22, 2021. The Company is currently commercializing FOTIVDA in the United States through the support of approximately 65 field-based employees, which includes approximately 50 oncology sales professionals targeting practicing oncologists. FOTIVDA is available to patients through a network of specialty pharmacies and distributors.

FOTIVDA, through the Company's partner EUSA Pharma (UK) Limited ("EUSA"), is also approved in the European Union ("EU"), New Zealand and South Africa and is reimbursed in the United Kingdom, Germany, Spain and certain other countries in EUSA's territory. FOTIVDA is approved in the EU for the first line treatment of adult patients with advanced RCC and for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for advanced RCC. FOTIVDA has been commercially available in the EU since 2017.

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, the Company is seeking to advance FOTIVDA in additional cancer indications with significant unmet medical needs. The Company is studying FOTIVDA in combination with immune checkpoint inhibitors for the treatment of hepatocellular carcinoma, or HCC, and RCC in phase 2 and phase 3 clinical trials.

The Company is conducting the DEDUCTIVE trial through a drug supply and cost sharing collaboration with AstraZeneca PLC ("AstraZeneca"). The DEDUCTIVE trial is an open-label, multi-center, randomized phase 1b/2 clinical trial of tivozanib in combination with IMFINZI (durvalumab), AstraZeneca's monoclonal antibody directed against programmed death-ligand 1 ("PD-L1") in the first-line treatment of patients with advanced, unresectable HCC who have not received prior systemic therapy.

The Company is also seeking to advance its pipeline of three wholly owned humanized immunoglobulin G1 ("IgG1") monoclonal antibody product candidates: ficlatuzumab, AV-380 and AV-203.

Ficlatuzumab is a potent humanized IgG1 monoclonal antibody that targets hepatocyte growth factor ("HGF"). The Company has previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck ("HNSCC") pancreatic cancer and acute myeloid leukemia ("AML"). The Company is currently conducting a randomized phase 2 confirmatory study of ficlatuzumab (the "Phase 2 HNSCC Trial"), for the potential treatment of HNSCC and it expects to receive top line data from the Phase 2 HNSCC Trial in the middle of 2021. The Company has initiated manufacturing of the clinical supply for a potential phase 3 clinical trial of ficlatuzumab, and it continues to evaluate opportunities for the further clinical development of ficlatuzumab.

AV-380 is a potent humanized IgG1 monoclonal antibody that targets growth differentiation factor 15 ("GDF15"). In December 2020, the FDA approved the Company's investigational new drug application ("IND") for AV-380 for the potential treatment of cancer cachexia, and, in the first quarter of 2021, the Company initiated a phase 1 clinical trial in healthy volunteers.

AV-203 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3) to which the Company will regain worldwide rights in September 2021. It is exploring AV-203 as a potential oncology treatment.

AV-353 is an IgG1 monoclonal antibody that targets the Notch 3 pathway.

As used throughout these condensed consolidated financial statements, the terms “AVEO,” and the “Company” refer to the business of AVEO Pharmaceuticals, Inc. and its three wholly-owned subsidiaries, AVEO Pharma Limited, AVEO Pharma (Ireland) Limited and AVEO Securities Corporation.

Liquidity and Going Concern

In accordance with Accounting Standards Update (“ASU”) No. 2014-15, *Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern* (Subtopic 205-40), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. The Company’s financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through March 31, 2021, the Company has financed its operations primarily through private placements and public offerings of its common stock and preferred stock, license fees, milestone payments and research and development funding from strategic partners, and loan proceeds. The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property and general and administrative functions relating to these operations.

The future success of the Company is dependent on its ability to commercialize FOTIVDA in the United States and to develop its clinical stage assets and, ultimately, upon the Company’s ability to create shareholder value. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. The Company’s future product revenues will depend upon the size of markets in which FOTIVDA, and any future products, have received approval, and its ability to achieve sufficient market acceptance, reimbursement from third-party payers and adequate market share for FOTIVDA and any future products in those markets. The likelihood of the Company’s long-term success must be considered in light of the expenses, difficulties and potential delays that may be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which the Company operates. Absent the realization of sufficient revenues from product sales to support the Company’s cost structure, the Company may never attain or sustain profitability.

The Company has incurred recurring losses and cash outflows from operations since its inception, including an accumulated deficit of $643.3 million as of March 31, 2021. The Company anticipates that it will continue to incur significant operating expenses for the foreseeable future as it commercializes FOTIVDA in the United States and continues its planned development activities for its clinical stage assets. The Company may require substantial additional funding to advance its pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources.

As of May 10, 2021, the date of issuance of these consolidated financial statements, the Company expects that its cash and cash equivalents of $121.4 million as of March 31, 2021, along with net product revenues from the commercial launch of FOTIVDA in the United States, will be sufficient to fund its current operations for more than twelve months from the date of filing this Quarterly Report on Form 10-Q.

Management’s expectations with respect to its ability to fund current planned operations is based on estimates that are subject to risks and uncertainties, including, without limitation, risks related to its ability to generate product revenue from sales of FOTIVDA in the United States, which became commercially available in the United States on March 22, 2021. If actual results are different from management’s estimates, the Company may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any of these strategic or financing opportunities would be executed or executed on favorable terms, and some could be dilutive to existing stockholders. If the Company is unable to obtain additional funding on a timely basis, it may be forced to significantly curtail, delay or discontinue one or more of its planned research or development programs or be unable to expand its operations or otherwise capitalize on its commercialization of its product and product candidates.

(2) Basis of Presentation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, AVEO Pharma Limited, AVEO Pharma (Ireland) Limited and AVEO Securities Corporation. The Company has eliminated all significant intercompany accounts and transactions in consolidation.

The accompanying condensed consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("GAAP") for interim financial information and with the instructions to Form 10-Q and Article 8 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. In the opinion of management, all adjustments, consisting of normal recurring accruals and revisions of estimates, considered necessary for a fair presentation of the condensed consolidated financial statements have been included. Interim results for the three months ended March 31, 2021 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2021 or any other future period.

The information presented in the condensed consolidated financial statements and related footnotes at March 31, 2021, and for the three months ended March 31, 2021 and 2020, is unaudited, and the condensed consolidated balance sheet amounts and related footnotes as of December 31, 2020 have been derived from the Company's audited financial statements. For further information, refer to the consolidated financial statements and accompanying footnotes included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020, which was filed with the U.S. Securities and Exchange Commission ("SEC") on March 16, 2021.

(3) Significant Accounting Policies

Revenue Recognition

Under Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers*, the Company recognizes revenue when its customers obtain control of promised goods or services, in an amount that reflects the consideration which the Company determines it expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract; and (v) recognize revenue when (or as) the Company satisfies its performance obligation(s). As part of the accounting for these arrangements, the Company must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Net Product Revenue

On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC after two prior systemic therapies. FOTIVDA became commercially available on March 22, 2021. FOTIVDA is the Company's first commercial product. The Company sells its products principally through a limited distribution network comprised of two specialty pharmacies, Biologics and Onco360, and the following specialty distributors: Amerisource Specialty Distribution, Oncology Supply, McKesson Plasma and Biologics, McKesson Specialty and Cardinal Specialty, or collectively, the Company's Customers. These Customers subsequently resell the Company's products to health care providers and patients. In addition to distribution agreements with Customers, the Company enters into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of the Company's products. Revenues from product sales are recognized when the Customer obtains control of the Company's product, which occurs at a point in time, typically upon delivery to the Customer.

Product Sales Discounts and Allowances

The Company records revenues from product sales at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established primarily from discounts, chargebacks, rebates, co-pay assistance, returns and other allowances that are offered within contracts between the Company and its Customers, health care providers, payors and other indirect customers relating to the sales of its products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is deductible by the Customer from payments to the Company) or a current liability (if the amount is payable by the Company to a third party or Customer). Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, forecasted Customer buying and payment patterns, and the Company's historical experience that will develop overtime as FOTIVDA is the Company's first commercial product. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of its contracts. The amount of variable consideration that 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 the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenues and earnings in the period such variances become known.

Chargebacks: Chargebacks are discounts that occur when contracted customers purchase directly from a specialty distributor. Contracted customers, which currently consist primarily of Public Health Service institutions, Federal government entities purchasing via the Federal Supply Schedule, Group Purchasing Organizations, and health maintenance organizations, generally purchase the product at a discounted price. The specialty distributor, in turn, charges back to the Company the difference between the price initially paid by the specialty distributor and the discounted price paid to the specialty distributor by its contracted customer. The allowance for chargebacks is based on actual chargebacks received and an estimate of sales by the specialty distributor to its contracted customers.

Discounts for Prompt Payment: The Company's Customers receive a discount of 2% for prompt payment. The Company expects its Customers will earn 100% of their prompt payment discounts and, therefore, the Company deducts the full amount of these discounts from total product sales when revenues are recognized.

Rebates: Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program, other government programs and commercial contracts. Rebate amounts owed after the final dispensing of the product to a benefit plan participant are based upon contractual agreements or legal requirements with public sector benefit providers, such as Medicaid. The allowance for rebates is based on statutory or contractual discount rates and expected utilization. The Company's estimates for the expected utilization of rebates are based on Customer and payer data received from the specialty pharmacies and distributors and historical utilization rates that will develop overtime as FOTIVDA is the Company's first commercial product. Rebates are generally invoiced by the payer and paid in arrears, such that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's shipments to the Company's Customers, plus an accrual balance for known prior quarters' unpaid rebates. If actual future rebates vary from estimates, the Company may need to adjust its accruals, which would affect net product revenues in the period of adjustment. Allowances for rebates also include amounts related to the Medicare Part D Coverage Gap Discount Program. In the United States during 2020, the Medicare Part D prescription drug benefit mandated participating manufacturers to fund 70% of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. The Company's estimates for expected Medicare Part D coverage gap amounts are based on Customer and payer data received from specialty pharmacies and distributors and historical utilization rates that will develop overtime as FOTIVDA is the Company's first commercial product. Funding of the coverage gap is invoiced and paid in arrears so that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's shipments to the Company's Customers, plus an accrual balance for known prior quarters' unpaid claims. If actual future funding varies from estimates, the Company may need to adjust its accruals, which would affect net product revenues in the period of adjustment.

Co-payment Assistance: Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. The Company accrues a liability for co-payment assistance based on actual program participation and estimates of program redemption using Customer data provided by the third party that administers the copay program.

Other Customer Credits: The Company pays fees to its Customers for account management, data management and other administrative services. To the extent the services received are distinct from the sale of products to its Customers, the Company classifies these payments in selling, general and administrative expenses in its Consolidated Statements of Income.

The following table summarizes net product revenues for FOTIVDA earned in the three months ended March 31, 2021 and 2020, respectively (in thousands).

	Three Months Ended March 31,	
	2021	2020
Product revenues:		
Gross product revenues	$ 1,256	$ —
Discounts and allowances	(190)	—
Net product revenues	$ 1,066	$ —

The following table summarizes the percentage of total product revenues for FOTIVDA by customer who individually accounted for 10% or more of total product revenues earned in the three months ended March 31, 2021 and 2020, respectively:

	Three Months Ended March 31,	
	2021	2020
OncoMed Specialty, LLC (Onco360)	31%	—
Affiliates of McKesson Corporation	33%	—
Affiliates of AmerisourceBergen Corporation	23%	—
Affiliates of Cardinal Health Specialty	13%	—
	100%	—

Product Sales Discounts and Allowances

The activities and ending allowance balances for each significant category of discounts and allowances for FOTIVDA (which constitute variable consideration) for the three months ended March 31, 2021 were as follows (in thousands):

	Chargebacks, Discounts for Prompt Pay and Other Allowances	Rebates, Customer Fees / Credits and Co-Pay Assistance	Totals
Provision related to sales made in:			
Current period	$ 112	$ 78	$ 190
Payments and customer credits issued	—	—	—
Balance at March 31, 2021	$ 112	$ 78	$ 190

The allowances for chargebacks, discounts for prompt payment and other allowances are recorded as a reduction of trade receivables, net, and the remaining reserves are recorded as rebates and fees due to customers in the accompanying Consolidated Balance Sheets.

Collaboration Revenues

The Company's historical revenues have been generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple promised goods and services, which may include (i) licenses, or options to obtain licenses, to the Company's technology, (ii) research and development activities to be performed on behalf of the collaborative partner, and (iii) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Collaboration Arrangements Within the Scope of ASC 808, Collaborative Arrangements

The Company analyzes its collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and are therefore within the scope of ASC Topic 808, *Collaborative Arrangements* ("ASC 808"). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements that are deemed to be within the scope of ASC 808, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606. The Company's policy is generally to recognize amounts received from collaborators in connection with joint operating activities that are within the scope of ASC 808 as a reduction in research and development expense.

Arrangements Within the Scope of ASC 606, Revenue from Contracts with Customers

Once a contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within the contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a

material right to the customer and if so, they are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed each of its revenue generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of its arrangements.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time based on the use of an output or input method.

Licenses of Intellectual Property: The terms of the Company's license agreements include the license of functional intellectual property, given the functionality of the intellectual property is not expected to change substantially as a result of the Company's ongoing activities. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from the portion of the transaction price allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises (that is, for licenses that are not distinct from other promised goods and services in an arrangement), the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and Development Funding: Arrangements that include payment for research and development services are generally considered to have variable consideration. If and when the Company assesses the payment for these services is no longer subject to the constraint on variable consideration, the related revenue is included in the transaction price.

Milestone payments: At the inception of each arrangement that includes non-refundable payments for contingent milestones, including preclinical research and development, clinical development and regulatory, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of the achievement of contingent milestones and the likelihood of a significant reversal of such milestone revenue, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and licensing revenue in the period of adjustment. This quarterly assessment may result in the recognition of revenue related to a contingent milestone payment before the milestone event has been achieved.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

The following table summarizes the total collaboration revenues earned in the three months ended March 31, 2021 and 2020, respectively, by partner (in thousands). Refer to Note 4, *"Collaborations and License Agreements"* regarding specific details.

	Three Months Ended March 31,	
	2021	**2020**
EUSA	$ 854	$ 784
Total	$ 854	$ 784

Trade Receivables

Trade receivables, net, includes amounts billed to the Company's customers for product sales of FOTIVDA. The Company records trade receivables net of chargebacks, cash discounts for prompt payment and any allowances for credit losses. The Company may apply an aging method to estimate credit losses and consider its own historical loss, if any, adjusted to account for current conditions, and reasonable and supportable forecasts of future economic conditions affecting its customers. The Company's Customers are specialty pharmacies and specialty distributors, and accordingly, the Company considers the risk of potential credit losses to be low.

Cost of Products Sold

Cost of products sold is related to our product revenues for FOTIVDA and consists primarily of tiered royalty payments the Company is required to pay to Kyowa Kirin Co. ("KKC") on all net sales of tivozanib in the Company's North American territory, which range from the low to mid-teens as a percentage of net sales. Refer to Note 4, *"Collaborations and License Agreements"* regarding specific details. Cost of products sold also consists of shipping and other third-party logistics and distribution costs for the Company's products. The Company considers regulatory approval of product candidates to be uncertain and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained. As such, the manufacturing costs for FOTIVDA incurred prior to regulatory approval were not capitalized as inventory, but were expensed as research and development costs.

Research and Development Expenses

Research and development expenses are charged to expense as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including (i) internal costs for salaries, bonuses, benefits, stock-based compensation, research-related overhead, and allocated expenses for facilities and information technology, and (ii) external costs for clinical trials, drug manufacturing and distribution, preclinical studies, upfront license payments, milestones and sublicense fees related to in-licensed products and technology, consultants and other contracted services.

Warrants Issued in Connection with Private Placement

In May 2016, the Company issued warrants to purchase an aggregate of 1,764,242 shares of common stock in connection with a private placement financing and recorded the warrants as a liability (the "PIPE Warrants"). The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. As of March 31, 2021, PIPE Warrants exercisable for 80,309 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding. Refer to Note 7, "*Common Stock—Private Placement – May 2016*" for further discussion of the private placement financing.

The PIPE Warrants contain a provision giving the warrant holder the option to receive cash, equal to the fair value of the remaining unexercised portion of the warrant, as cash settlement in the event that there is a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, *Distinguishing Liabilities from Equity* requires that these warrants be classified as a liability and not as equity. Accordingly, the Company recorded a warrant liability in the amount of approximately $9.3 million upon issuance of the PIPE Warrants. The fair value of these warrants has been determined using the Black-Scholes pricing model. These warrants are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net until the earlier of their exercise or expiration or upon the completion of a liquidation event. Upon exercise, the PIPE Warrants are subject to revaluation just prior to the date of the warrant exercise and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net and the corresponding reduction in the PIPE Warrant liability is recorded as additional paid-in capital in the Balance Sheet as a component of stockholder's equity.

The Company recorded a non-cash loss of approximately $2.4 million in the three months ended March 31, 2021 in its Statement of Operations attributable to the increase in the fair value of the warrant liability that resulted from a higher stock price as of March 31, 2021 relative to prior periods, an increase in the Company's stock volatility rate and a shorter remaining term as the PIPE Warrants approach their scheduled expiration on May 16, 2021. The Company recorded a non-cash gain of approximately $2.6 million in the three months ended March 31, 2020 in its Statement of Operations attributable to the decrease in the fair value of the warrant liability that resulted from a lower stock price as of March 31, 2020 relative to prior periods. No PIPE Warrants were exercised during the three months ended March 31, 2021 and 2020.

The following table rolls forward the fair value of the Company's PIPE Warrant liability, the fair value of which is determined by Level 3 inputs for the three months ended March 31, 2021 (in thousands):

Fair value at January 1, 2021	$	199
Increase in fair value		2,396
Fair value at March 31, 2021	$	2,595

The key assumptions used to value the PIPE Warrants were as follows:

	Issuance	December 31, 2020	March 31, 2021
Expected price volatility	76.25%	56.79%	159.96%
Expected term (in years)	5.00	0.50	0.25
Risk-free interest rates	1.22%	0.09%	0.03%
Stock price	$ 8.90	$ 5.77	$ 7.32
Dividend yield	—	—	—

Cash, Cash Equivalents and Marketable Securities

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase and an investment in a United States government money market fund to be cash equivalents. Changes in the balance of cash and cash equivalents may be affected by changes in investment portfolio maturities, as well as actual cash disbursements to fund operations.

The Company's cash is deposited in highly-rated financial institutions in the United States. The Company invests in United States government money market funds, high-grade, short-term commercial paper, corporate bonds and other United States government agency securities, which management believes are subject to minimal credit and market risk. The carrying values of the Company's cash and cash equivalents approximate fair value due to their short-term maturities.

The Company does not have any restricted cash balances.

Marketable Securities

Marketable securities consist primarily of investments which have expected average maturity dates in excess of three months. The Company invests in high-grade corporate obligations, including commercial paper, and United States government and government agency obligations that are classified as available-for-sale. Since these securities are available to fund current operations they are classified as current assets on the consolidated balance sheets.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive income or loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. The cost of marketable securities is adjusted for amortization of premiums and accretion of discounts, with such amortization and accretion recorded as a component of interest expense, net. Realized gains and losses are determined on the specific identification method. Unrealized gains and losses are included in other comprehensive loss until realized, at which point they would be recorded as a component of interest expense, net.

Below is a summary of cash, cash equivalents and marketable securities at March 31, 2021 and December 31, 2020 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
March 31, 2021				
Cash and cash equivalents:				
Cash and money market funds	$ 121,414	$ —	$ —	$ 121,414
Total cash, cash equivalents and marketable securities	**$ 121,414**	**$ —**	**$ —**	**$ 121,414**
December 31, 2020				
Cash and cash equivalents:				
Cash and money market funds	$ 61,761	$ —	$ —	$ 61,761
Total cash, cash equivalents and marketable securities	**$ 61,761**	**$ —**	**$ —**	**$ 61,761**

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to credit risk primarily consist of cash and cash equivalents, marketable securities and accounts receivable. The Company maintains deposits in highly-rated, federally-insured financial institutions in excess of federally insured limits. The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the high credit quality standards outlined in the Company's investment policy. This policy also limits the amount of credit exposure to any one issue or type of instrument.

The Company's trade receivables, net, includes amounts billed to the Company's customers for product sales of FOTIVDA, which is the Company's first commercial product that was approved by the FDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC after two prior systemic therapies. The Company's Customers are a limited group of specialty pharmacies and specialty distributors, and accordingly, the Company considers the risk of potential credit losses to be low.

The Company's partnership receivables include amounts due to the Company from licensees and collaborators. The Company has not experienced any material losses related to partnership receivables from individual licensees or collaborators.

Fair Value Measurements

The fair value of the Company's financial assets and liabilities reflects the Company's estimate of amounts that it would have received in connection with the sale of the assets or paid in connection with the transfer of the liabilities in an orderly transaction between market participants at the measurement date. In connection with measuring the fair value of its assets and liabilities, the Company seeks to maximize the use of observable inputs (market data obtained from sources independent from the Company) and to minimize the use of unobservable inputs (the Company's assumptions about how market participants would price assets and liabilities). The following fair value hierarchy is used to classify assets and liabilities based on the observable inputs and unobservable inputs used in order to value the assets and liabilities:

Level 1: Quoted prices in active markets for identical assets or liabilities. An active market for an asset or liability is a market in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2: Observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3: Unobservable inputs based on the Company's assessment of the assumptions that market participants would use in pricing the asset or liability.

Financial assets and liabilities are classified in their entirety within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The Company measures the fair value of its marketable securities by taking into consideration valuations obtained from third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker-dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities and other observable inputs.

As of March 31, 2021, the Company had financial assets valued based on Level 1 inputs consisting of cash and cash equivalents in a United States government money market fund. During the three months ended March 31, 2021, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of March 31, 2021, the Company's financial liability that was recorded at fair value consisted of the PIPE Warrant liability.

The fair value of the Company's loans payable at March 31, 2021 and December 31, 2020 approximates its carrying value, computed pursuant to a discounted cash flow technique using a market interest rate and is considered a Level 3 fair value measurement. The effective interest rate, which reflects the current market rate, considers the loan issuance costs and the deferred financing charge.

The following table summarizes the financial assets and liabilities measured at fair value on a recurring basis at March 31, 2021 and December 31, 2020 (in thousands):

	Fair Value Measurements as of March 31, 2021			
	Level 1	Level 2	Level 3	Total
Financial assets carried at fair value:				
Cash and money market funds	$ 121,414	$ —	$ —	$ 121,414
Total cash, cash equivalents and marketable securities	**$ 121,414**	**$ —**	**$ —**	**$ 121,414**
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	**$ —**	**$ —**	**$ 2,595**	**$ 2,595**

	Fair Value Measurements as of December 31, 2020			
	Level 1	Level 2	Level 3	Total
Financial assets carried at fair value:				
Cash and money market funds	$ 61,761	$ —	$ —	$ 61,761
Total cash, cash equivalents and marketable securities	**$ 61,761**	**$ —**	**$ —**	**$ 61,761**
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	**$ —**	**$ —**	**$ 199**	**$ 199**

Basic and Diluted Net Loss per Common Share

Basic net income (loss) per share attributable to the Company's common stockholders is based on the weighted-average number of common shares outstanding during the period. Diluted net income (loss) per share attributable to the Company's common stockholders is based on the weighted-average number of common shares outstanding during the period plus additional weighted-average common equivalent shares outstanding during the period when the effect is dilutive.

For the three months ended March 31, 2021 and 2020, diluted net loss per share is the same as basic net loss per share as the inclusion of weighted-average shares of common stock issuable upon the exercise of outstanding stock options and warrants would be anti-dilutive. In each of the three months ended March 31, 2021 and 2020, the average market prices of the Company's common stock were below the exercise prices of $10.00 and $12.50 per share for the PIPE Warrants and Offering Warrants, respectively.

The following table summarizes outstanding securities not included in the computation of diluted net loss per common share as the effect would have been anti-dilutive for the three months ended March 31, 2021 and 2020, respectively (in thousands):

	Outstanding at March 31,	
	2021	2020
Stock options outstanding	3,068	1,556
Offering Warrants outstanding	2,253	2,500
PIPE Warrants outstanding	1,684	1,684
Total	7,005	5,740

Stock-Based Compensation

Under the Company's stock-based compensation programs, the Company periodically grants stock options and restricted stock to employees, directors and nonemployee consultants. The Company also issues shares under an employee stock purchase plan. The fair value of each award is recognized in the Company's statements of operations over the requisite service period for such award.

Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. The Company uses the Black-Scholes option pricing model to value its stock option awards without market conditions, which requires the Company to make certain assumptions regarding the expected volatility of its common stock price, the expected term of the option grants, the risk-free interest rate and the dividend yield with respect to its common stock. The Company calculates volatility using its historical stock price data. Due to the lack of the Company's own historical data, the Company elected to use the "simplified" method for "plain vanilla" options to estimate the expected term of the Company's stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. The risk-free interest rate used for each grant is based on the United States Treasury yield curve in effect at the time of grant for instruments with a similar expected life. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends.

The fair value of equity-classified awards to employees and directors is measured at fair value on the date the awards are granted. During the three months ended March 31, 2021 and 2020, the Company recorded the following stock-based compensation expense (in thousands):

	Three Months Ended March 31,	
	2021	2020
Research and development	$ 355	$ 115
Selling, general and administrative	849	428
Total	$ 1,204	$ 543

Income Taxes

The Company provides for income taxes using the asset-liability method. Under this method, deferred tax assets and liabilities are recognized based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company calculates its provision for income taxes on ordinary income based on its projected annual tax rate for the year. Uncertain tax positions are recognized if the position is more-likely-than-not to be sustained upon examination by a tax authority. Unrecognized tax benefits represent tax positions for which reserves have been established. As of March 31, 2021, the Company is forecasting an effective tax rate of 0% for the year ending December 31, 2021. The Company maintains a full valuation allowance on all deferred tax assets.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment principally in the United States. As of March 31, 2021, the Company has no net assets located outside of the United States.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect certain reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, the assessment of the Company's ability to continue as a going concern, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, clinical trial costs and contract research accruals, measurement of trade receivables net, measurement of the PIPE Warrant liability, measurement of stock-based compensation and estimates of the Company's capital requirements over the next twelve months from the date of issuance of the consolidated financial statements. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Material changes in these estimates could occur in the future. Changes in estimates are recorded or reflected in the Company's disclosures in the period in which they become known. Actual results could differ from those estimates if past experience or other assumptions do not turn out to be substantially accurate.

Accrued Clinical Trial Costs and Contract Research Liabilities

During each of the three months ended March 31, 2021 and 2020, the Company had arrangements with multiple contract research organizations ("CROs") whereby these organizations commit to performing services for the Company over multiple reporting periods. The Company recognizes the expenses associated with these arrangements based on its expectation of the timing of the performance of components under these arrangements by these organizations. Generally, these components consist of the costs of setting up the trial, monitoring the trial, closing the trial and preparing the resulting data. Costs related to patient enrollment in clinical trials are accrued as patients are enrolled in the trial.

In addition to fees earned by the CROs to manage the Company's clinical trials, the CROs are also responsible for managing payments to the clinical trial sites on the Company's behalf. There can be significant lag time in clinical trial sites invoicing the CROs. The date on which services are performed, the level of services performed and the cost of such services are often determined based on subjective judgments. The Company makes these judgments based upon the facts and circumstances known to it, such as the terms of the contract and its knowledge of activity that has been incurred, including the number of active clinical sites, the number of patients enrolled, the activities to be performed for each patient, including patient treatment and any imaging, if applicable, the activities to be performed for each patient, and the duration for which the patients will be enrolled in the trial. In the event that the Company does not identify some costs which have begun to be incurred, or the Company under or overestimates the level of services performed or the costs of such services in a given period, its reported expenses for such period would be understated or overstated. The Company currently reflects the effects of any changes in estimates based on changes in facts and circumstances directly in its operations in the period such change becomes known.

With respect to financial reporting periods presented in this Quarterly Report on Form 10-Q, the timing of the Company's actual costs incurred have not differed materially from its estimated timing of such costs.

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The Company adopted ASU 2019-02 effective January 1, 2021. The adoption of this standard did not have a material impact on the Company's consolidated financial statements.

(4) Collaborations and License Agreements

Collaboration Agreement

AstraZeneca

In December 2018, the Company entered into a clinical supply agreement (the "AstraZeneca Agreement") with a wholly-owned subsidiary of AstraZeneca PLC ("AstraZeneca") to evaluate the safety and efficacy of AstraZeneca's IMFINZI (durvalumab), a human monoclonal antibody directed against programmed death-ligand 1 ("PD-L1"), in combination with tivozanib as a first-line treatment for patients with advanced, unresectable HCC in an open-label, multi-center, randomized phase 1b/2 clinical trial (the "DEDUCTIVE trial"). The Company serves as the study sponsor; each party contributes the clinical supply of its study drug; key decisions are made by both parties by consensus; and external study costs are otherwise shared equally.

The Company is accounting for the joint development activities under the AstraZeneca Agreement as a joint risk-sharing collaboration in accordance with ASC 808 because both the Company and AstraZeneca are active participants in the oversight of the

DEDUCTIVE trial via their participation on a joint steering committee and are exposed to significant risk and rewards in connection with the activity based on their obligation to share in the costs. AstraZeneca does not meet the definition of a customer, thus the joint development activities under the AstraZeneca Agreement are not accounted for under ASC 606.

Payments from AstraZeneca with respect to its share of the external costs for the DEDUCTIVE trial incurred by the Company pursuant to a joint development plan are recorded as a reduction in research and development expenses due to the joint risk-sharing nature of the activities that is not representative of a vendor-customer relationship.

The Company records reimbursements from AstraZeneca for external study costs as a reduction in research and development expense during the period that reimbursable expenses are incurred. As a result of the cost sharing provisions in the AstraZeneca Agreement, the Company's research and development expenses were reduced by approximately $0.2 million and $0.4 million in the three months ended March 31, 2021 and 2020, respectively. The amount due to the Company from AstraZeneca pursuant to the cost-sharing provision was approximately $0.4 million as of March 31, 2021.

Out-License Agreements

CANbridge

In March 2016, the Company entered into a collaboration and license agreement (the "CANbridge Agreement") with CANbridge Life Sciences, Ltd. ("CANbridge"). Under the terms of the CANbridge Agreement, the Company granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, the Company's potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3), for the diagnosis, treatment and prevention of disease in all countries outside of North America.

Pursuant to the CANbridge Agreement, CANbridge made an upfront payment to the Company of $1.0 million in April 2016, net of $0.1 million of foreign withholding taxes. CANbridge also reimbursed the Company for $1.0 million of certain AV-203 manufacturing costs incurred by the Company prior to entering into the CANbridge Agreement. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, one in March 2017 and one in September 2017, net of foreign withholding taxes, following CANbridge's validation of the manufacturing process for AV-203 for clinical use. In December 2017, CANbridge filed an IND application with the National Medical Products Administration (formerly, the China Food and Drug Administration) ("NMPA") for a clinical study of AV-203, which CANbridge referred to as CAN017, in esophageal squamous cell carcinoma ("ESCC"). In August 2018, CANbridge obtained regulatory approval of this IND application from the NMPA and, accordingly, the Company earned a $2.0 million development and regulatory milestone payment that was received from CANbridge in August 2018. No further clinical development or additional milestones were achieved by CANbridge as of March 31, 2021.

A percentage of any milestone and royalty payments received by the Company pursuant to the CANbridge Agreement, excluding upfront and reimbursement payments, or under future partnership agreements related to the AV-203 program, were due to Biogen Idec International GmbH ("Biogen") as a sublicensing fee under the option and license agreement between the Company and Biogen dated March 18, 2009, as amended. The $2.0 million development and regulatory milestone the Company earned in August 2018 for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018.

In March 2021, CANbridge exercised its right to terminate for convenience the CANbridge Agreement. Under the terms of the CANbridge Agreement, the Company expects the transfer of the AV-203 program to be complete in September 2021 and, at that time, the Company will regain worldwide rights to the AV-203 program.

EUSA

In December 2015, the Company entered into an agreement (the "EUSA Agreement"), under which the Company granted to EUSA the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa and Australasia (collectively, the "EUSA Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye.

EUSA made research and development reimbursement payments to the Company of $2.5 million upon the execution of the EUSA Agreement during the year ended December 31, 2015 and $4.0 million in September 2017 upon its receipt of marketing approval from the European Commission in August 2017 for FOTIVDA (tivozanib) for the treatment of RCC. In September 2017, EUSA elected to opt-in to co-develop the phase 2 clinical trial of tivozanib in combination with OPDIVO (nivolumab), a PD-1 inhibitor, in the first-line and the second-line treatment of RCC (the "TiNivo trial"). As a result of exercising its opt-in right, EUSA made an additional research and development reimbursement payment to the Company of $2.0 million. This $2.0 million payment was received in October 2017, in advance of the completion of the TiNivo trial, and represented EUSA's approximate 50% share of

the total costs of the TiNivo trial. The Company is also eligible to receive an additional research and development reimbursement payment from EUSA of 50% of the total costs for the Company's phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, sorafenib (Nexavar®), in 350 subjects in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies, including subjects with prior checkpoint inhibitor therapy (the"TIVO-3 trial"), up to $20.0 million, if EUSA elects to opt-in to that study.

The Company is entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy, Spain and the United Kingdom (collectively, the "EU5"). The Company is also entitled to receive an additional $2.0 million for the grant of marketing approval for RCC, if any, in three of the licensed countries outside of the EU, as mutually agreed by the parties, of which approvals have been obtained in New Zealand in July 2019 and in South Africa in September 2020. In February 2018, November 2018 and February 2019, EUSA obtained reimbursement approval from the National Institute for Health and Care Excellence ("NICE") in the United Kingdom, the German Federal Association of the Statutory Health Insurances ("GKV-SV") in Germany and the Ministry of Health, Consumer Affairs and Social Welfare ("MSCBS") in Spain, respectively, for the first-line treatment of RCC. Accordingly, the Company earned a $2.0 million milestone payment with respect to reimbursement approval in the United Kingdom that was received in March 2018, a $2.0 million milestone payment with respect to reimbursement approval in Germany that was received in December 2018 and a $2.0 million milestone payment with respect to reimbursement approval in Spain that was received in May 2019. The Company is also eligible to receive a payment of $2.0 million per indication in connection with a filing by EUSA with the European Medicines Agency ("EMA") for marketing approval, if any, for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as potentially up to $335.0 million upon EUSA's achievement of certain sales thresholds. The Company is also eligible to receive tiered double-digit royalties on net sales, if any, of licensed products in the EUSA Licensed Territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. No milestone payments nor research and development reimbursement payments were earned in the three months ended March 31, 2021 and 2020.

The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KKC, subject to certain limitations. The Company, however, would owe KKC 30% of other, non-research and development payments it may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in the EU5, marketing approvals for RCC in three specified non-EU Licensed Territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties, as set forth above. The $2.0 million milestone payments the Company earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approval for FOTIVDA from the NICE in the United Kingdom, the GKV-SV in Germany and the MSCBS in Spain, respectively, for the first-line treatment of RCC were subject to the 30% KKC sublicense fee, or $0.6 million, each. The sublicense fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout the EUSA Licensed Territories in RCC. EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the EUSA Licensed Territories.

Accounting Under ASC 606

Under ASC 606, the upfront consideration and regulatory milestones included in the transaction price are being recognized as collaboration and licensing revenue over the Company's substantive performance period from contract execution in December 2015 through April 2022. Under ASC 606, upon the achievement of a regulatory milestone, the amount that represents the cumulative catch-up for the period from contract execution in December 2015 through the date of the milestone achievement is recognized as collaboration and licensing revenue, with the balance classified as deferred revenue and recognized as collaboration and licensing revenue over the remainder of the performance period, currently estimated through April 2022.

None of the remaining regulatory-related milestones are included in the transaction price as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) the remaining reimbursement and marketing approvals in RCC are outside of the control of EUSA and vary on a country-by-country basis, (ii) milestones related to the submission filings for EMA approval of tivozanib in up to three additional indications are contingent upon the success of future clinical trials in additional indications, if any, and are outside of the control of EUSA, (iii) milestones related to the marketing approval by the EMA for tivozanib in up to three additional indications are contingent upon the success of the corresponding future clinical trials, if any, and are outside of the control of EUSA, and (iv) efforts by EUSA.

Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to EUSA and therefore are recognized at the later of when the performance obligation is satisfied (or partially satisfied) or the related sales occur. The Company will re-evaluate the transaction price, including its estimated variable consideration for milestones included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

In November 2017, the Company began earning sales royalties upon EUSA's commencement of the first commercial launch of FOTIVDA (tivozanib) with the initiation of product sales in Germany. EUSA has received reimbursement approval for and commercially launched FOTIVDA in Germany, the United Kingdom, and Spain as well as in some additional non-EU5 countries. EUSA is working to secure reimbursement approval in Italy and France and commercially launch FOTIVDA in additional European countries. The Company recognized royalty revenue of approximately $0.4 million and $0.3 million in the three months ended March 31, 2021 and 2020, respectively.

The Company recognized total revenues under the EUSA Agreement of approximately $0.9 million and $0.8 million in the three months ended March 31, 2021 and 2020, respectively. As of March 31, 2021, there was approximately $2.1 million in total deferred revenue that is expected to continue to be recognized as collaboration and licensing revenue, in the approximate amount of $0.5 million per quarter, over the duration of the Company's performance period, currently estimated through April 2022.

The following table summarizes the revenues earned in connection with the EUSA Agreement under ASC 606 for the three months ended March 31, 2021 and 2020 (in thousands):

		Three Months Ended March 31,	
Revenue Type	**Date Achieved**	**2021**	**2020**
Collaboration and Licensing Revenue:			
Amounts in contract liabilities at the beginning of the period:			
Upfront payment	December 2015	$ 98	$ 98
R&D payment - EMA approval in RCC	August 2017	158	158
Milestone - UK reimbursement approval	February 2018	79	79
Milestone - German reimbursement approval	November 2018	79	79
Milestone - Spanish reimbursement approval	February 2019	79	79
		$ 493	$ 493
Partnership Royalties		361	291
Total		$ 854	$ 784

The following table summarizes changes in the Company's accounts receivable and contract liabilities (deferred revenue) in connection with the EUSA Agreement for the three months ended March 31, 2021 (in thousands):

Contract Assets	**Beginning Balance January 1, 2021**	**Additions**	**Deductions**	**Ending Balance March 31, 2021**
Partnership receivables	$ 392	$ 361	$ —	$ 753

				Deferred Revenue			
Contract Liabilities	**Transaction Price**	**Date Achieved**	**Date Paid**	**Beginning Balance January 1, 2021**	**Additions**	**Deductions**	**Ending Balance March 31, 2021**
Amounts in contract liabilities at the beginning of the period:							
Upfront payment	$ 2,500	December 2015	December 2015	$ 512	$ —	$ (98)	$ 414
R&D payment - EMA approval in RCC	4,000	August 2017	September 2017	817	—	(158)	659
Milestone - UK reimbursement approval	2,000	February 2018	March 2018	408	—	(79)	329
Milestone - German reimbursement approval	2,000	November 2018	December 2018	407	—	(79)	328
Milestone - Spanish reimbursement approval	2,000	February 2019	May 2019	408	—	(79)	329
Total	$ 12,500			$ 2,552	$ —	$ (493)	$ 2,059

Biodesix

In April 2014, the Company entered into a worldwide co-development and collaboration agreement (the "Biodesix Agreement") with Biodesix, Inc. ("Biodesix") to develop and commercialize ficlatuzumab, the Company's potent humanized IgG1 monoclonal antibody that targets HGF. Under the Biodesix Agreement, prior to the first commercial sale of ficlatuzumab, each party had the right to elect to discontinue its funding obligation for further development or commercialization efforts with respect to ficlatuzumab in exchange for reduced economics in the program, which is referred to as an "Opt-Out." In September 2020, the Company regained full global rights to ficlatuzumab, effective December 2, 2020, when Biodesix exercised its "Opt-Out" rights under the Biodesix Agreement.

The Company and Biodesix are currently funding an investigator-sponsored clinical trial for ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC. The Biodesix Agreement generally provided for each party to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab and to share equally in any future revenue from development or commercialization.

Pursuant to the terms of the Biodesix Agreement, as a result of Biodesix's election to Opt-Out, Biodesix will (i) continue to be responsible for reimbursement of development costs with respect to the ongoing open label Phase 2 investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC (the "Phase 2 HNSCC Trial"), (ii) cease to be entitled to 50% sharing of profits resulting from commercialization of ficlatuzumab, (iii) be entitled to a low double digit royalty on future product sales and 25% of future licensing revenue (excluding contributions to research and development expenses) less approximately $2.5 million that Biodesix would be required to pay to the Company pursuant to the October 2016 amendment to the Biodesix Agreement and (iv) remain responsible for development obligations under the Biodesix Agreement with respect to VeriStrat. Biodesix and the Company also remain obligated to negotiate a commercialization agreement to delineate their rights and obligations in the event of any commercialization of VeriStrat with ficlatuzumab. As a result of Biodesix's decision to Opt-Out, the Company now has worldwide licensing rights and sole decision-making authority with respect to further development and commercialization of ficlatuzumab. The payment obligations between the parties under the Biodesix Agreement are in effect until completion of the Phase 2 HNSCC Trial.

The Company is accounting for the joint development activities under the Biodesix Agreement as a joint risk-sharing collaboration in accordance with ASC 808 because both the Company and Biodesix have been active participants in the ongoing development of ficlatuzumab via their participation on a joint steering committee that oversaw the development plans for ficlatuzumab and have been exposed to significant risk and rewards in connection with their activity based on their obligations to share in the costs, as defined above. Payments from Biodesix with respect to its share of ficlatuzumab development costs incurred by the Company pursuant to a joint development plan are recorded as a reduction in research and development expenses due to the joint risk-sharing nature of the activities that is not representative of a vendor-customer relationship.

The Company records reimbursements from Biodesix for expenses related to these trials and drug manufacturing as a reduction in research and development expense during the period that reimbursable expenses are incurred. As a result of the cost sharing provisions in the Biodesix Agreement, the Company reduced research and development expenses by approximately $0.1 million and $0.6 million in the three months ended March 31, 2021 and 2020, respectively. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was approximately $0.2 million as of March 31, 2021.

Biogen Idec International GmbH

In March 2009, the Company entered into an exclusive option and license agreement with Biogen regarding the development and commercialization of the Company's discovery-stage ErbB3-targeted antibodies, including AV-203, for the potential treatment and diagnosis of cancer and other diseases outside of North America (the "Biogen Agreement"). Under the Biogen Agreement, the Company was responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, would generate data sufficient to support advancement to a phase 3 clinical trial.

In March 2014, the Company and Biogen amended the Biogen Agreement (the "Biogen Amendment"). Pursuant to the Biogen Amendment, Biogen agreed to the termination of its rights and obligations under the Biogen Agreement, including Biogen's option to (i) obtain a co-exclusive (with the Company) worldwide license to develop and manufacture ErbB3 targeted antibodies and (ii) obtain exclusive commercialization rights to ErbB3 products in countries in the world other than North America. As a result, the Company has worldwide rights to AV-203. Pursuant to the Biogen Amendment, the Company was obligated to use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The Company is also obligated to pay Biogen a percentage of milestone payments received by the Company from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, if any, up to a cumulative maximum amount of $50.0 million.

In March 2016, the Company entered into a collaboration and license agreement for AV-203 with CANbridge, which satisfied its obligation to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The $2.0 million development and regulatory milestone the Company earned in August 2018 in connection with CANbridge's regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018. See "*—CANbridge*" within this Note 4 for a further description of that arrangement.

In-License Agreements

St. Vincent's

In July 2012, the Company entered into a license agreement with St. Vincent's, under which the Company obtained an exclusive, worldwide sublicensable right to research, develop, manufacture and commercialize products for human therapeutic, preventative and palliative applications that benefit from inhibition or decreased expression or activity of GDF15, which is also referred to as MIC-1 (the "St. Vincent's Agreement"). Under the St. Vincent's Agreement, St. Vincent's also granted the Company non-exclusive rights for certain related diagnostic products and research tools.

In order to sublicense certain necessary intellectual property rights to Novartis in August 2015, the Company amended and restated the St. Vincent's Agreement and made an additional upfront payment to St. Vincent's of $1.5 million. As of March 31, 2021, the Company is required to make future milestone payments, up to an aggregate total of $14.4 million, upon the earlier of the achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third indications, for licensed therapeutic products, some of which payments may be increased by a mid to high double-digit percentage rate for milestone payments made after the Company grants any sublicense, depending on the sublicensed territory. The Company will also be required to pay St. Vincent's tiered royalty payments equal to a low-single-digit percentage of any net sales it or its sublicensees make from licensed therapeutic products. The royalty rate escalates within the low-single-digit range during each calendar year based on increasing licensed therapeutic product sales during such calendar year.

Kyowa Kirin Co. (KKC)

In December 2006, the Company entered into an agreement with KKC (the "KKC Agreement"), under which it obtained an exclusive, sublicensable license to develop, manufacture and commercialize tivozanib in all territories in the world except for Asia and the Middle East, where KKC retained the rights to tivozanib. Under the KKC Agreement, the Company obtained exclusive rights to tivozanib in its territory under certain KKC patents, patent applications and know-how for the diagnosis, prevention and treatment of all human diseases and conditions (the "Field"). On August 1, 2019, the Company entered into an amendment to the KKC Agreement pursuant to which KKC repurchased the non-oncology rights to tivozanib in the Company's territory, excluding the rights the Company has sublicensed to EUSA under the EUSA Agreement. The Company has upfront, milestone and royalty payment obligations to KKC under the KKC Agreement related to the amended Field for oncology development by the Company, and following the amendment, KKC also has upfront, milestone and royalty payment obligations to the Company related to non-oncology development by KKC in the Company's territory. Pursuant to the amendment to the KKC Agreement, KKC was required to make a non-refundable upfront payment to the Company in the amount of $25.0 million that was received in September 2019 and KKC waived a one-time milestone payment of $18.0 million otherwise payable by the Company upon obtaining marketing approval for tivozanib in the United States.

KKC Agreement

Upon entering into the KKC Agreement, the Company made an upfront payment in the amount of $5.0 million. In March 2010, the Company made a milestone payment to KKC in the amount of $10.0 million in connection with the dosing of the first patient in the Company's TIVO-1 trial. In December 2012, the Company made a $12.0 million milestone payment to KKC in connection with the acceptance by the FDA of the Company's 2012 NDA filing for tivozanib. Each milestone under the KKC Agreement is a one-time only payment obligation, accordingly, the Company did not owe KKC another milestone payment in connection with the dosing of the first patient in the Company's TIVO-3 trial, and did not owe a milestone payment to KKC when the Company filed its NDA with the FDA on March 31, 2020. Pursuant to the amendment to the KKC Agreement, KKC waived a one-time milestone payment of $18.0 million otherwise payable by the Company upon obtaining marketing approval for tivozanib in the United States. The Company has no remaining development and commercialization milestone payments due to KKC under the KKC Agreement.

If the Company sublicenses any of its rights to tivozanib to a third party, as it has done with EUSA, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under the KKC Agreement relating to rights the Company retains. The Company is required to pay KKC a fixed 30% of amounts the Company receives from its sublicensees, including upfront license fees, milestone payments and royalties, but excluding amounts the Company receives in respect of research and development reimbursement payments or equity investments, subject to certain limitations. Certain research and development reimbursement payments by EUSA, including the $2.5 million upfront payment in December 2015, the $4.0 million payment in September 2017 upon the receipt of marketing authorization from the European Commission for FOTIVDA and the $2.0 million payment upon EUSA's election in September 2017 to opt-in to co-develop the TiNivo trial, were not subject to sublicense revenue payments to KKC. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of 50% of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KKC, subject to certain limitations. The Company would, however, owe KKC 30% of other, non-research and development payments the Company may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in up to five specified EU countries, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties. The $2.0 million milestone payments the Company earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approvals for FOTIVDA as a first-line treatment for RCC in the United Kingdom, Germany and Spain, respectively, were subject to the 30% KKC sublicense fee, or $0.6 million each. The sublicense fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

The Company is also required to pay tiered royalty payments on net sales it makes of tivozanib in its North American territory, which range from the low to mid-teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. The Company's royalty payment obligations in a particular country in its territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC after two prior systemic therapies. On March 22, 2021, the Company commenced product sales of FOTIVDA. In the three months ended March 31, 2021, the Company recognized approximately $0.1 million in royalties due to KKC on net product sales of FOTIVDA in its Statement of Operations as a component of cost of products sold.

The Company and KKC each have access to and can benefit from the other party's clinical data and regulatory filings with respect to tivozanib and biomarkers identified in the conduct of activities under the KKC Agreement, as related to the amended Field for oncology development. Under the KKC Agreement, the Company is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in its territory.

The KKC Agreement will remain in effect until the expiration of all of the Company's royalty and sublicense revenue obligations, determined on a product-by-product and country-by-country basis, unless terminated earlier. If the Company fails to meet its obligations under the KKC Agreement and is unable to cure such failure within specified time periods, KKC can terminate the KKC Agreement, resulting in a loss of our rights to tivozanib and an obligation to assign or license to KKC any intellectual property or other rights the Company may have in tivozanib, including its regulatory filings, regulatory approvals, patents and trademarks for tivozanib.

August 1, 2019 Amendment to the KKC Agreement

In addition to the non-refundable upfront payment to the Company pursuant to the amendment to the KKC Agreement in the amount of $25.0 million and the waiver of the $18.0 million milestone for US approval of tivozanib, KKC is also required to make milestone payments to the Company of up to an aggregate of $390.7 million upon the successful achievement of certain development and sales milestones of tivozanib in non-oncology indications. On August 2, 2020, KKC's IND application for a non-oncology use of tivozanib was accepted by the Pharmaceuticals and Medical Devices Agency of Japan. Accordingly, the Company earned a $2.8 million development milestone payment upon acceptance of the IND pursuant to the KKC Agreement that was received in August 2020. In addition, KKC is required to make tiered royalty payments to the Company on net sales of tivozanib in non-oncology indications in the Company's territory, which range from high single digit to low double digits as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales, subject to certain adjustments. KKC's royalty payment obligations in a particular country in the Company's territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of the expiration date of the last valid claim of a patent application or patent owned by KKC covering tivozanib or 10 years after the date of first commercial sale of tivozanib in non-oncology indications in that country. No milestone payments were earned in the three months ended March 31, 2021 and 2020.

If KKC sublicenses any of its rights to tivozanib to a third-party, KKC is required to pay the Company a percentage of amounts received from the respective sublicensees related to the Company's territory, including upfront license fees, milestone payments and royalties, but excluding amounts received in respect of research and development reimbursement payments or equity investments, subject to certain limitations.

Accounting Analysis Under the August 1, 2019 Amendment to the KKC Agreement

Following the repurchase of non-oncology rights by KKC, the amended KKC Agreement is accounted for as two distinct agreements: (i) the KKC Agreement by which the Company has upfront, milestone and royalty payment obligations to KKC related to the Company's oncology development of tivozanib in the amended Field for the Company's territory that continues to be accounted for under ASC 730, *Research and Development*, and (ii) the amended KKC Agreement by which KKC has upfront, milestone and royalty payment obligations to the Company related to its non-oncology development of tivozanib for the Company's territory that will be accounted for under ASC 606.

The Company evaluated the amendment to the KKC Agreement under ASC 606 and determined that KKC met the definition of a customer as the Company considers the licensing or sale of intellectual property rights to be an output of the Company's ordinary activities and is central to the operations of the Company. The Company determined that the amendment to the KKC Agreement contained a single performance obligation related to the Company's transfer of rights to non-oncology intellectual property and know-how to KKC, excluding the rights the Company has sublicensed to EUSA under the EUSA Agreement. In addition, the Company determined that the $25.0 million non-refundable upfront payment received from KKC in September 2019 constituted the amount of the consideration to be included in the transaction price and attributed this amount to the Company's single performance obligation. The Company satisfied this performance obligation during the third quarter of 2019. Accordingly, the Company recognized the $25.0 million in consideration as revenue in the third quarter of 2019. The Company concluded the performance obligation was satisfied at a point in time because any know-how or clinical data generated from the Company's ongoing oncology development of tivozanib would not benefit KKC's non-oncology development of tivozanib.

In the third quarter of 2020, the Company increased the transaction price to $27.8 million to include the $2.8 million development milestone that was earned in August 2020 upon the acceptance of KKC's IND application for a non-oncology use of tivozanib by the Pharmaceuticals and Medical Devices Agency of Japan. Accordingly, the Company recognized the $2.8 million in consideration as revenue in the third quarter of 2020 as the Company did not have any ongoing performance obligations under the amendment to the KKC Agreement.

None of KKC's remaining development and regulatory milestones to the Company related to its non-oncology development of tivozanib for the Company's territory were included in the transaction price, as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) regulatory approvals are outside of the control of KKC, (ii) certain development and regulatory milestones are contingent upon the success of future clinical trials, if any, which is out of the control of KKC, and (iii) efforts by KKC. Any consideration related to development and regulatory milestones owed by KKC to the Company will be recognized when the corresponding milestones are no longer constrained as the Company does not have any ongoing performance obligations. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the intellectual property transferred to KKC and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur.

(5) Other Accrued Liabilities

Other accrued expenses consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Professional fees	$ 1,931	$ 1,061
Compensation and benefits	1,668	3,082
Other	1,124	320
Total	$ 4,723	$ 4,463

(6) Hercules Loan Facility

On May 28, 2010, the Company entered into a loan and security agreement (the "First Loan Agreement") with Hercules Capital Inc. and certain of its affiliates ("Hercules"). The First Loan Agreement was subsequently amended in March 2012, September 2014, May 2016 and amended and restated in December 2017 (the "2017 Loan Agreement").

On August 7, 2020, the Company entered into a first amendment to the 2017 Loan Agreement (the "2020 Loan Amendment") to provide the Company, subject to certain terms and conditions, with an additional term loan in an aggregate principal amount of up to $35.0 million (the "2020 Loan Facility") in up to four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement, and for general working capital purposes.

The Company received the initial $15.0 million of the 2020 Loan Facility upon the closing of the 2020 Loan Amendment, of which approximately $9.7 million was used to retire the then outstanding balance under the 2017 Loan Agreement and of which approximately $5.3 million was new loan funding which was used for general working capital purposes.

The remainder of the loan amount will be available to the Company, at its option, subject to certain terms and conditions, including upon the achievement of the following milestones: (i) the second tranche of $10.0 million ("Tranche Two") would be available through June 30, 2021 upon achieving FDA approval of FOTIVDA ("Performance Milestone I"), (ii) the third tranche of $5.0 million ("Tranche Three") would be available from July 1, 2021 through January 31, 2022 assuming the Company achieves $20.0 million in net product revenues from sales of FOTIVDA, by no later than December 31, 2021 ("Performance Milestone II"), and (iii) the fourth tranche of $5.0 million would be available through June 30, 2022 contingent upon the achievement of both Performance Milestone I and Performance Milestone II, and subject to the consent of Hercules.

The 2020 Loan Amendment also amended the 2017 Loan Agreement by: (i) extending maturity until September 1, 2023, which is extendable to September 1, 2024 at the Company's option assuming the Tranche Three funding has occurred, (ii) providing for an interest-only period beginning on the closing date of 2020 Loan Amendment and ending on September 30, 2021, which period may be extended through September 30, 2022 provided the Company achieved Performance Milestone I and further extendable through March 31, 2023 after the Tranche Three funding has occurred, if at all, and (iii) revising the per annum interest rate to the greater of (x) 9.65% and (y) an amount equal to 9.65% plus the prime rate as reported in the Wall Street Journal minus 3.25% as determined daily, provided however, that the per annum interest rate shall not exceed 15%. Principal payments are scheduled to commence on October 1, 2021, at the earliest, as described above. The interest rate as of March 31, 2021 was 9.65%.

Per the terms of the 2020 Loan Facility, principal will be repaid in equal monthly installments following the conclusion of the interest-only period. The Company may prepay all of the outstanding principal and accrued interest under the 2020 Loan Facility, subject to a prepayment charge up to 3.0% in the first year following the closing of the 2020 Loan Amendment, decreasing to 2.0% in year two and 1.0% in year three. The Company is obligated to make an end-of-term payment of 6.95% of the aggregate amount of loan funding received under the 2020 Loan Facility on the earlier of the maturity of the loan or the date on which the Company prepays any outstanding loan balance. The approximate $0.8 million end-of-term payment under the 2017 Loan Agreement continues to be due on July 1, 2021. In connection with the 2020 Loan Amendment, the Company incurred approximately $0.3 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2020 Loan Amendment was accounted for as a loan modification in accordance with ASC 470-50.

The 2020 Loan Facility includes various financial and operating covenants, including that the Company maintain an unrestricted cash position of at least $10.0 million through the date the Third Tranche funding is received and at least $5.0 million thereafter through the maturity of the loan. The Company is also required to achieve greater than or equal to 75% of its forecasted net product revenues from its sales of tivozanib over a 6-month trailing period, as defined and measured on a monthly basis, effective upon the Third Tranche funding and continuing through the maturity of the loan. The net product revenue covenant will not apply at any time the Third Tranche funding has not been provided nor such advance has been prepaid in full.

On February 1, 2021, the Company entered into the second amendment to the 2017 Loan Agreement (the "2021 Loan Amendment"), which increases the 2020 Loan Facility from up to $35.0 million to up to $45.0 million following FDA approval of FOTIVDA. The 2021 Loan Amendment makes certain changes to the 2020 Loan Amendment, including, among other things, (i) increasing Tranche Two funding upon achieving Performance Milestone I from $10.0 million to $20.0 million, thereby increasing the total amount of unfunded term loan commitments under the 2020 Loan Facility from $20.0 million to $30.0 million, (ii) increasing the amount of net product revenues from sales of FOTIVDA required to achieve Performance Milestone II from $20.0 million to $35.0 million and changing the deadline for achieving Performance Milestone II from December 31, 2021 to April 1, 2022 and (iii) increasing the amount of the financial covenant for the maintenance of an unrestricted cash position from at least $10.0 million to at least $15.0 million from the date the Tranche Two funding is received until the date the Tranche Three funding is received and at least

$10.0 million thereafter through the maturity of the Loan Agreement. In connection with the 2021 Loan Amendment, the Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount.

On March 11, 2021, the Company completed the $20.0 million drawdown of Tranche Two funding under the 2021 Loan Amendment that was made available in connection with the achievement of Performance Milestone I upon FDA approval of FOTIVDA on March 10, 2021. The achievement of Performance Milestone I extended the interest-only period by twelve months from September 30, 2021 to September 30, 2022 and increased the amount of unrestricted cash required for the Company to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million.

As of March 31, 2021, the total principal balance was $35.0 million, principal payments are scheduled to commence on October 1, 2022 and the corresponding end-of-term payments under the 2020 Loan Facility, in the aggregate amount of approximately $2.4 million, are due upon the current loan maturity date of September 1, 2023. The unamortized discount to be recognized over the remainder of the loan period was approximately $2.6 million and $1.2 million as of March 31, 2021 and December 31, 2020, respectively. Per the 2017 Loan Agreement, the end-of-term payment of approximately $0.8 million continues to be due on July 1, 2021.

The 2020 Loan Facility is secured by substantially all of the Company's assets, excluding intellectual property. The 2020 Loan Facility provides that certain events shall constitute a default by the Company, including failure by the Company to pay amounts under the 2020 Loan Amendment when due; breach or default in the performance of any covenant under the 2020 Loan Amendment by the Company, subject to certain cure periods; insolvency of the Company and certain other bankruptcy proceedings involving the Company; default by the Company of obligations involving indebtedness in excess of $500,000; and the occurrence of an event or circumstance that would have a material adverse effect upon the business of the Company. As of March 31, 2021, the Company was in compliance with all loan covenants, Hercules has not asserted any events of default and the Company does not believe that there has been a material adverse effect as defined in the 2020 Loan Amendment.

The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal as a long-term liability based on the timing of scheduled principal payments.

Future minimum payments under the loans payable outstanding as of March 31, 2021 are as follows (in thousands):

Year Ending December 31:	
2021 (remaining nine months)	3,316
2022	11,785
2023	30,097
	45,198
Less amount representing interest	(6,976)
Less unamortized discount	(2,563)
Less deferred charges	(3,222)
Less loans payable current, net of discount	—
Loans payable, net of current portion and discount	$ 32,437

(7) Common Stock

As of March 31, 2021, the Company had 50,000,000 authorized shares of common stock, $0.001 par value, of which 34,360,775 shares were issued and outstanding.

Public Offering – March 2021

On March 26, 2021, the Company completed an underwritten public offering of 6,900,000 shares of its common stock, including the full exercise by the underwriters of their option to purchase an additional 900,000 shares, at the public offering price of $8.00 per share for gross proceeds of approximately $55.2 million. The net offering proceeds to the Company were approximately $51.6 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

Universal Shelf Registration Statement

On November 9, 2020, the Company filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of up to $300.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "2020

Shelf"). The 2020 Shelf (File No. 333-249982) was declared effective by the SEC on November 18, 2020 and was filed to replace the Company's then existing shelf registration statement, which was terminated. As of March 31, 2021, there was approximately $213.0 million available for future issuance of common stock, preferred stock, debt securities, warrants and/or units.

Public Offering – June 2020

On June 19, 2020, the Company completed an underwritten public offering of 9,725,000 shares of its common stock, including the partial exercise by the underwriters of their option to purchase an additional 1,225,000 shares, at the public offering price of $5.25 per share for gross proceeds of approximately $51.1 million. Three stockholders beneficially holding more than 5% of the Company's voting securities, including an entity affiliated with New Enterprise Associates and two other stockholders, purchased an aggregate of 4,503,571 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of the Company's voting securities. The net offering proceeds to the Company were approximately $47.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

Public Offering – April 2019 (Offering Warrant Expiration – April 8,2021)

In April 2019, the Company completed an underwritten public offering of 2,173,913 shares of its common stock and warrants to purchase an aggregate of 2,500,000 shares of its common stock ("the Offering Warrants"), including warrants to purchase an aggregate of 326,086 shares of its common stock sold pursuant to the underwriter's partial exercise of its overallotment option, at the public offering price of $11.40 per share and $0.10 per warrant for gross proceeds of approximately $25.0 million. The Offering Warrants were immediately exercisable upon issuance at an exercise price of $12.50 per share, subject to adjustment in certain circumstances, and expired two years from the date of issuance on April 8, 2021. Any Offering Warrants that had not been exercised for cash prior to their expiration were to be automatically exercised via cashless exercise on the expiration date. The shares and warrants were issued separately and were separately transferable. An entity affiliated with New Enterprise Associates purchased 434,782 shares and warrants to purchase an aggregate of 434,782 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of the Company's voting securities. The net offering proceeds to the Company were approximately $22.8 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. The Company determined the shares of common stock and the Offering Warrants represented freestanding financial instruments. In addition, the Company conducted an assessment of the classification of the Offering Warrants and, based on their terms, concluded the Offering Warrants were equity-classified. Accordingly, the net offering proceeds of $22.8 million were recorded within stockholders' equity (deficit).

In March 2021, Offering Warrants exercisable for 247,391 shares of common stock had been exercised, for approximately $3.1 million in cash proceeds, and Offering Warrants exercisable for 2,252,609 shares of common stock were outstanding as of March 31, 2021. On April 8, 2021, all of the remaining 2,252,609 Offering Warrants expired and no shares of the Company's common stock were issued via automatic cashless exercises of unexercised warrants on the date of expiration as the $12.50 exercise price was greater than the Company's closing stock price of $7.01 on April 8, 2021.

Sales Agreement with SVB Leerink

In February 2018, the Company entered into a sales agreement with SVB Leerink LLC ("SVB Leerink" and the "SVB Leerink Sales Agreement") pursuant to which the Company may issue and sell shares of its common stock from time to time up to an aggregate amount of $50.0 million, at its option, through SVB Leerink as its sales agent, with any sales of common stock through SVB Leerink being made by any method that is deemed an "at-the-market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the "Securities Act"), or in other transactions pursuant to an effective shelf registration statement on Form S-3. The Company agreed to pay SVB Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the SVB Leerink Sales Agreement. The Company sold 470,777 shares, 1,251,555 shares, 1,070,175 shares and 330,688 shares pursuant to the SVB Leerink Sales Agreement, resulting in proceeds net of commissions of approximately $10.3 million, $7.5 million, $5.9 million and $3.4 million in the fourth quarter of 2018, February 2019, November 2020 and March 2021, respectively. As of March 31, 2021, approximately $22.2 million was available for issuance in connection with future stock sales pursuant to the SVB Leerink Sales Agreement.

Private Placement – May 2016 (PIPE Warrant Expiration - Scheduled on May 16, 2021)

In May 2016, the Company entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which the Company sold 1,764,242 units, at a price of $9.65 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of the Company's common stock and a warrant to purchase one share of the Company's common stock (the "PIPE Warrants"). The PIPE Warrants have an exercise price of

$10.00 per share and are exercisable for a period of five years from the date of issuance until their scheduled expiration on May 16, 2021. Certain of the Company's directors and executive officers purchased an aggregate of 54,402 units in this offering at the same price as the other investors. The net offering proceeds to the Company were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by the Company. As of March 31, 2021, PIPE Warrants exercisable for 80,309 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding.

(8) Stock-based Compensation

Stock Incentive Plan

The Company previously maintained the 2010 Stock Incentive Plan (the "2010 Plan") for employees, consultants, advisors, and directors, as amended in March 2013, June 2014 and June 2017.

In April 2019, the Company's board of directors adopted the 2019 Equity Incentive Plan (the "2019 Plan") and on June 12, 2019 the stockholders approved the 2019 Plan at the Annual Meeting of Stockholders. The 2019 Plan provides similar terms as the 2010 Plan, including: (i) a provision for the grant of equity awards such as stock options and restricted stock, (ii) that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the grant for participants who own less than 10% of the total combined voting power of stock of the Company and not less than 110% for participants who own more than 10% of the total combined voting power of the stock of the Company, (iii) that options and restricted stock granted under the 2019 Plan vest over periods as determined by the board of directors, which generally are equal to four years, and (iv) that options granted under the 2019 Plan expire over periods as determined by the board of directors, which generally are ten years from the date of grant. In April 2020, the board of directors adopted an amendment to the 2019 Plan to increase the total number of shares reserved under the Plan by 1,300,000 shares, among other things. The amendment was approved by stockholders at the Annual Meeting of Stockholders held on June 10, 2020.

Awards may be made under the 2019 Plan for up to the sum of (i) 2,300,000 shares of common stock and (ii) such additional number of shares of common stock (up to 1,068,901 shares) as is equal to (x) the number of shares of common stock reserved for issuance under the 2010 Plan that were available for grant under the 2010 Plan immediately prior to the date the 2019 Plan was approved by the Company's stockholders and (y) the number of shares of common stock subject to awards outstanding under the 2010 Plan, which awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company pursuant to a contractual repurchase right. As of March 31, 2021, there were 292,420 shares of common stock available for future issuance under the 2019 Plan and no shares of common stock available for future issuance under the 2010 Plan.

The following table summarizes stock option activity during the three months ended March, 31, 2021:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2021	1,816,690	$ 11.04	7.53	$ 170,000
Granted	1,308,138	$ 9.02		
Exercised	—	$ —		
Forfeited	(57,276)	$ 8.73		
Outstanding at March 31, 2021	3,067,552	$ 10.22	8.16	$ 1,634,000
Exercisable at March 31, 2021	1,061,401	$ 13.79	5.67	$ 566,000

The aggregate intrinsic value is based upon the Company's closing stock price of $7.32 on March 31, 2021.

The fair value of stock options subject only to service or performance conditions that are granted to employees is estimated on the date of grant using the Black-Scholes option-pricing model using the assumptions noted in the table below.

	Three Months Ended March 31,	
	2021	2020
Volatility factor	56.17% - 102.66%	94.37% - 94.51
Expected term (in years)	0.25 - 6.25	6.25
Risk-free interest rates	0.06% - 1.13%	1.52% - 1.67%
Dividend yield	—	—

The risk-free interest rate is determined based upon the United States Treasury's rates for United States Treasury zero-coupon bonds with maturities similar to those of the expected term of the options being valued. The Company does not expect to pay dividends in the foreseeable future.

Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the three months ended March 31, 2021 and 2020 was $7.03 and $4.50, respectively.

As of March 31, 2021, there was $12.7 million of total unrecognized stock-based compensation expense related to stock options granted to employees under the Plan. The expense is expected to be recognized over a weighted-average period of 3.4 years.

(9) Legal Proceedings

The Company evaluates developments in legal proceedings on a quarterly basis. The Company records an accrual for loss contingencies to the extent that the Company concludes that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated.

As of the date of filing this Quarterly Report on Form 10-Q, there are no outstanding legal proceedings against the Company or its current officers or directors.

Item 2.
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 elsewhere in this Quarterly Report on Form 10-Q and the audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2020, or Annual Report.

Overview

We are an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. Our strategy is to focus our resources on the development and commercialization of our product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. With the approval of our first commercial product, FOTIVDA® (tivozanib), in the United States, we have transitioned from a clinical development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company.

FOTIVDA is our lead product and was approved by the U.S. Food and Drug Administration, or FDA, for marketing and sale in the United States on March 10, 2021. FOTIVDA is approved in the United States for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma following two or more prior systemic therapies. FOTIVDA is an oral, next-generation vascular endothelial growth factor receptor, or VEGFR, tyrosine kinase inhibitor, or TKI. The FDA approval of FOTIVDA is based on our pivotal phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, Nexavar® (sorafenib), in renal cell carcinoma, or RCC, patients whose disease had relapsed or become refractory to two or three prior systemic therapies, which we refer to as the TIVO-3 trial. The approval is also supported by three additional trials in RCC and includes safety data from over 1,000 clinical trial subjects.

FOTIVDA became commercially available in the United States on March 22, 2021. We are currently commercializing FOTIVDA in the United States through the support of approximately 65 field-based employees, which includes approximately 50 oncology sales professionals targeting practicing oncologists. The field force is supported by the AVEO ACE Patient Support program, which is an extensive patient and healthcare provider support program designed to optimize patient access and help patients navigate their treatment journey. In light of the restrictions necessitated by the COVID-19 pandemic, we designed our strategic commercial approach to be optimized for remote as well as in-person customer engagement capabilities and expanded our digital marketing strategies. FOTIVDA is available to patients through a network of specialty pharmacies and distributors.

We believe there is significant commercial opportunity for FOTIVDA in the United States. We estimate that the current U.S. market for relapsed or refractory RCC therapy is approximately $1.0 billion, including $700 million in the second line and $300 million in the third and fourth lines. As the TIVO-3 trial is the first positive phase 3 study in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies as well as the first phase 3 study in RCC to investigate a predefined subpopulation of patients who received prior immunotherapy, a predominant standard of care for earlier lines of therapy, we believe that FOTIVDA could become a standard of care in the United States in this relapsed or refractory setting.

FOTIVDA, through our partner EUSA Pharma (UK) Limited, or EUSA, is also approved in the European Union, or the EU, New Zealand and South Africa and is reimbursed in the United Kingdom, Germany, Spain and certain other countries in EUSA's territory. FOTIVDA is approved in the EU for the first line treatment of adult patients with advanced RCC and for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for advanced RCC. FOTIVDA has been commercially available in the EU since 2017. EUSA has not commercially launched FOTIVDA in France, Germany, Italy or Spain. EUSA is working to secure reimbursement approval in and commercially launch FOTIVDA in additional EU countries. However, there is significant competition in the front-line RCC setting in the EU due to the approval of several immunotherapy combinations which have become a standard of care and impacted the market opportunity for monotherapy treatments. EUSA has reported to us that to date, it has not experienced a decrease in sales trends or interruptions in supply or distribution of FOTIVDA during the COVID-19 pandemic; however, the future impact of the COVID-19 pandemic on FOTIVDA sales is difficult to predict.

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, we are seeking to advance FOTIVDA in additional cancer indications with significant unmet medical needs. We are studying FOTIVDA in combination with immune checkpoint inhibitors for the treatment of hepatocellular carcinoma, or HCC, and RCC in phase 2 and phase 3 clinical trials.

We are conducting the DEDUCTIVE trial through a drug supply and cost sharing collaboration with AstraZeneca PLC, or AstraZeneca. The DEDUCTIVE trial is an open-label, multi-center, randomized phase 1b/2 clinical trial of tivozanib in combination

with IMFINZI (durvalumab), AstraZeneca's monoclonal antibody directed against programmed death-ligand 1, or PD-L1, in the first-line treatment of patients with advanced, unresectable HCC who have not received prior systemic therapy. In January 2021, we presented preliminary results from the phase 1b portion of the DEDUCTIVE trial in a poster session at the 2021 American Society of Clinical Oncology Gastrointestinal, or ASCO GI, Cancers Symposium.

We plan to initiate enrollment in the middle of 2021 in a phase 3 study, which we refer to as the TiNivo-2 Trial, in collaboration with Bristol-Myers Squibb Company, or BMS. We are the sponsor of the study and BMS is supplying OPDIVO® (nivolumab), BMS's anti-PD-1 therapy, for the study. The TiNivo-2 Trial is a randomized, open-label, controlled phase 3 clinical trial of FOTIVDA in combination with OPDIVO®, in patients with advanced relapsed or refractory RCC following prior immunotherapy exposure. We recently received feedback from the FDA regarding the trial design and we expect to commence enrollment in the trial in the middle of 2021.

We are also seeking to advance our pipeline of three wholly owned humanized immunoglobulin G1, or IgG1, monoclonal antibody product candidates: ficlatuzumab, AV-380 and AV-203.

Ficlatuzumab is a potent humanized IgG1 monoclonal antibody that targets hepatocyte growth factor, or HGF. We have previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck, or HNSCC, pancreatic cancer and acute myeloid leukemia, or AML. We are currently conducting a randomized phase 2 confirmatory study of ficlatuzumab, or the Phase 2 HNSCC Trial, for the potential treatment of HNSCC and we expect to receive top line data from the Phase 2 HNSCC Trial in the middle of 2021. We have initiated manufacturing of the clinical supply for a potential phase 3 clinical trial of ficlatuzumab, and we continue to evaluate opportunities for the further clinical development of ficlatuzumab.

AV-380 is a potent humanized IgG1 monoclonal antibody that targets growth differentiation factor 15, or GDF15. In December 2020, the FDA approved our investigational new drug application, or IND, for AV-380 for the potential treatment of cancer cachexia, and, in the first quarter of 2021, we initiated a phase 1 clinical trial in healthy volunteers.

AV-203 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3) to which we will regain worldwide rights in September 2021. We are exploring AV-203 as a potential oncology treatment.

AV-353 is an IgG1 monoclonal antibody that targets the Notch 3 pathway.

Business *Update Regarding COVID-19.* The pandemic caused by an outbreak of a new strain of coronavirus, or the COVID-19 pandemic, that is affecting the U.S. and global economy and financial markets is also impacting our employees, patients, communities and business operations to varying degrees. In the paragraphs that follow, we have described impacts of the COVID-19 pandemic on our commercialization plans and clinical development programs, as applicable. The extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets. Certain of our operations had been conducted remotely prior to the COVID-19 pandemic, and we have now transitioned essentially all of our business operations to be conducted remotely in response to COVID-19. If the COVID-19 pandemic continues or becomes more severe, it may further impact our ability to maintain that level of productivity, to grow the company as we have anticipated and to execute our commercialization and other long-term business strategies. Management is actively monitoring this situation and the possible effects on our financial condition, liquidity, operations, suppliers, industry and workforce. For additional information on risks posed by the COVID-19 pandemic, please see "Part II, Item 1A. Risk Factors – Risks Related to the COVID-19 Pandemic," included elsewhere in this Quarterly Report on Form 10-Q.

Financial Overview

We do not have a history of generating operating profits and, as of March 31, 2021, we had an accumulated deficit of $643.3 million. We anticipate that we will continue to incur significant operating expenses for the foreseeable future as we seek to successfully commercialize FOTIVDA in the United States and continue our planned development activities for our clinical stage assets.

We may require substantial additional funding to continue to advance our pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources. Please see "Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources —Liquidity and Going Concern" for a further discussion of our funding requirements.

Revenue

Our revenues have historically been generated primarily through collaborative research, development and commercialization agreements. Payments to us under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales. In November 2017, we began earning sales royalties upon EUSA's commencement of the first commercial launch of FOTIVDA (tivozanib). In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property.

On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. We commenced commercial sales of our first product FOTIVDA in the United States on March 22, 2021. We expect that any revenue we generate will fluctuate from quarter to quarter and year to year as a result of the timing and amount of the payments that we receive upon the sales of FOTIVDA and any future products, to the extent any are successfully commercialized, and license fees, research and development reimbursements, milestones, royalties and other payments received under our strategic partnerships. If we or our strategic partners fail to complete the development of our product candidates in a timely manner or to obtain or maintain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

Research and development expenses have historically consisted of expenses incurred in connection with the discovery and development of our product candidates. We recognize research and development expenses as they are incurred. These expenses consist primarily of:

- employee-related expenses, including salaries, bonuses, benefits, stock-based compensation and research-related overhead;
- external development-related expenses, including clinical trials, preclinical studies, consultants and other outsourced services;
- costs of acquiring and manufacturing drug development related materials and related distribution;
- costs associated with our regulatory and quality assurance operations and medical affairs;
- upfront license payments, milestones, sublicense fees and royalties related to in-licensed products and technology; and
- allocated expenses for facilities and information technology.

Research and development expenses are net of amounts reimbursed under our agreements with Biodesix and AstraZeneca for their respective shares of development costs incurred by us under our joint development plans with each respective partner.

We anticipate that research and development expenses will increase in 2021, principally related to increases for a full year of costs for the medical affairs function in support of the commercial launch of FOTIVDA, ficlatuzumab manufacturing of clinical supply for a potential phase 3 clinical trial in HNSCC, the planned TiNivo-2 trial for the treatment of advanced relapsed or refractory RCC and the conduct of the phase 1 clinical trial of AV-380 in healthy volunteers. These increases will be partially offset by lower costs, principally related to the TIVO-3 trial as it nears completion and costs incurred in 2020 related to the submission of our tivozanib new drug application, or NDA, in March 2020 and related FDA review support that will not be incurred in 2021. The timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Currently, we track direct external development expenses and direct salary on a program-by-program basis and allocate general-related expenses, such as indirect compensation, benefits and consulting fees, to each program based on the personnel resources allocated to such program. Facilities, IT costs and stock-based compensation are not allocated amongst programs and are considered overhead.

Uncertainties of Estimates Related to Research and Development Expenses

The process of conducting preclinical studies and clinical trials necessary to obtain FDA approval for each of our product candidates is costly and time-consuming. The probability of success for each product candidate and clinical trial may be affected by a variety of factors, including, among others, the risk benefit profile of the product candidates' clinical activity, investment in the program, competition, manufacturing capabilities and commercial viability.

At this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates, or the period, if any, in which material net cash inflows may commence from sales of any approved products. This uncertainty is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- our ability to establish and maintain strategic partnerships, the terms of those strategic partnerships and the success of those strategic partnerships, if any, including the timing and amount of payments that we might receive from strategic partners;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any product candidate;
- the progress and results of our clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the emergence of competing technologies and products and other adverse market developments;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; and
- additional manufacturing requirements.

As a result of the uncertainties associated with developing drugs, including those discussed above, we are unable to determine the exact duration and completion costs of current or future clinical stages of our product candidates, or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates for which we may obtain regulatory approval. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success, if any, of each product candidate, as well as ongoing assessment of each product candidate's commercial potential. We will need to raise substantial additional capital in the future in order to fund the development of our preclinical and clinical product candidates.

Selling, General and ***Administrative Expenses***

Selling, general and administrative expenses consist principally of compensation, benefits and travel for employees in executive, finance, legal, human resource and commercial functions. Other selling, general and administrative expenses include professional fees for audit, tax, general legal, patent legal, investor relations, commercial, consulting services and directors' fees, as well as facility and information technology-related costs not otherwise included in research and development expenses.

We anticipate that selling, general and administrative expenses associated with the commercialization of FOTIVDA will continue to increase significantly during the first half of the year principally related to the addition of our salesforce, and continued expansion of our marketing, market access and commercial capabilities and general and administrative support, and will remain consistent at that level in the second half of 2021. Accordingly, the timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Interest Expense, Net

Interest expense consists of interest, amortization of debt discount, and amortization of deferred financing costs associated with our loans payable, and is shown net of interest income, which consists of interest earned on our cash, cash equivalents and marketable securities. The primary objective of our investment policy is capital preservation.

Income Taxes

We calculate our provision for income taxes on ordinary income based on our projected annual tax rate for the year. As of March 31, 2021, we are forecasting an effective tax-rate of 0% for the year ending December 31, 2021, and since we maintain a full valuation allowance on all of our deferred tax assets, we have recorded no income tax provision or benefit in the current quarter.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of financial statements in conformity

with GAAP requires us to make estimates and assumptions that affect certain reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, the assessment of our ability to continue as a going concern, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, clinical trial costs and contract research accruals, measurement of trade receivables net, measurement of the PIPE Warrant liability, measurement of stock-based compensation and estimates of our capital requirements over the next twelve months from the date of issuance of the consolidated financial statements. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Material changes in these estimates could occur in the future. Changes in estimates are recorded or reflected in our disclosures in the period in which they become known. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate. Our significant accounting policies are described in the notes to our consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

For a discussion of recent accounting pronouncements, refer to Note 3 – "*Significant Accounting Policies – Recently Adopted Accounting Pronouncements*", to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Results of Operations

Comparison of Three Months Ended March 31, 2021 and 2020

Revenues (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
FOTIVDA product revenue, net	$ 1,066	$ —	$ 1,066	100%
Partnership revenue - EUSA	854	784	70	9%
Total revenues	$ 1,920	$ 784	$ 1,136	145%

Our total revenues increased by $1.1 million, or 145%, to $1.9 million in the three months ended March 31, 2021 from $0.8 million in the same period in 2020, principally due to the commencement of commercial sales of our first product FOTIVDA in the United States on March 22, 2021 for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies.

Partnership revenues from EUSA increased by $70,000, or 9%, in the three months ended March 31, 2021 from the same period in 2020.

FOTIVDA Product Revenue, Net (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
Gross product revenue	$ 1,256	$ —	$ 1,256	100%
Discounts and allowances	(190)	—	(190)	100%
Product revenue, net	$ 1,066	$ —	$ 1,066	100%

We commenced commercial sales of our first product FOTIVDA in the United States on March 22, 2021 for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies.

Cost of Products Sold (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
Cost of products sold	$ 138	$ —	$ 138	100%
Gross margin %	87%	—	87%	100%

We commenced commercial sales of our first product FOTIVDA in the United States on March 22, 2021 for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. Cost of products sold is related to our product revenues for FOTIVDA and consists primarily of tiered royalty payments we are required to pay to Kyowa Kirin Co. (KKC) on all net sales of tivozanib in our North American territory, which range from the low to mid-teens as a percentage of net sales. Cost of products sold also consists of shipping and other third-party logistics and distribution costs for FOTIVDA. We consider regulatory approval of our product candidates to be uncertain and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained. As such, the manufacturing costs for FOTIVDA incurred prior to regulatory approval were not capitalized as inventory but were expensed as research and development costs, which favorably impacted our gross margin. We anticipate that gross margins will be in the mid-to-high 80th percentile for the remainder of 2021.

Research and Development Expenses (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
Tivozanib	$ 3,856	$ 6,161	$ (2,305)	(37)%
AV-380	766	718	48	7%
Ficlatuzumab	450	579	(129)	(22)%
Overhead	725	368	357	97%
Total research and development expenses	$ 5,797	$ 7,826	$ (2,029)	(26)%

Our total research and development expenses decreased by $2.0 million, or 26%, to $5.8 million in the three months ended March 31, 2021 from $7.8 million in the same period in 2020, principally due to a decrease of $2.3 million in tivozanib-related expenses.

Tivozanib expenses decreased by $2.3 million, or 37%, in the three months ended March 31, 2021 as compared to the same period in 2020. The $2.3 million decrease was principally related to $3.7 million in costs incurred in the first quarter of 2020 that were not incurred in the first quarter of 2021 related to the tivozanib NDA for RCC, including $0.8 million related to the completion of the NDA submission and the $2.9 million application user fee pursuant to the Prescription Drug User Fee Act that was due upon the filing of the tivozanib NDA on March 31, 2020, and $0.5 million related to lower expenses in connection with the TIVO-3 trial as it nears completion, partially offset by $1.6 million in costs incurred in the first quarter of 2021 that were not incurred in the first quarter of 2020, including $1.1 million related to the conduct of start-up activities for the planned TiNivo-2 trial and $0.5 million related to the medical affairs function in support of the commercial launch of FOTIVDA.

AV-380 expenses increased by $48,000, or 7%, in the three months ended March 31, 2021 as compared to the same period in 2020, principally due to the commencement of the phase 1 clinical trial of AV-380 in healthy volunteers in the first quarter of 2021, partially offset by a decrease in pre-clinical development costs incurred in the first quarter of 2020 that were not incurred in the first quarter of 2021.

Ficlatuzumab expenses decreased by $0.1 million, or 22%, in the three months ended March 31, 2021 as compared to the same period in 2020, principally due to an increase of $0.4 million related to the conduct of ficlatuzumab manufacturing of clinical supply for a potential phase 3 clinical trial in HNSCC, offset by a $0.5 million decrease related to costs incurred in the first quarter of 2020 that were not incurred in the first quarter of 2021 in connection with the discontinued phase 2 clinical trial evaluating ficlatuzumab in combination with high-dose cytarabine versus high-dose cytarabine alone in patients with AML, which we referred to as the CyFi-2 trial, net of cost sharing with Biodesix.

We anticipate that research and development expenses will increase in 2021, principally related to increases for a full year of costs attributable to the medical affairs function supporting the commercial launch of FOTIVDA, ficlatuzumab manufacturing of clinical supply for a potential phase 3 clinical trial in HNSCC, the planned TiNivo-2 trial for the treatment of advanced relapsed or refractory RCC and the conduct of the phase 1 clinical trial of AV-380 in healthy volunteers. These increases will be partially offset by lower costs, principally related to the TIVO-3 trial as it nears completion and costs incurred in 2020 related to the submission of our tivozanib NDA in March 2020 and related FDA review support that will not be incurred in 2021. The timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Selling, General and Administrative Expenses (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
Selling, general and administrative expenses	$ 15,100	$ 3,672	$ 11,428	311%

Selling, general and administrative expenses increased by $11.4 million, or 311%, to $15.1 million in the three months ended March 31, 2021 from $3.7 million in the same period in 2020. The $11.4 million increase was principally due to $11.3 million in total increases, including: (i) $9.4 million in commercial launch-readiness initiatives incurred in the first quarter of 2021 that were not incurred in the same period in 2020, including $4.6 million in compensation and recruiting costs related to the growth in our commercial infrastructure, including the hiring of the salesforce, and $4.8 million related to external commercial-launch readiness activities in marketing, market access and commercial operations, (ii) $1.1 million in other professional fees, and (iii) $0.8 million in other compensation-related costs.

We anticipate that selling, general and administrative expenses associated with the commercialization of FOTIVDA will continue to increase significantly during the first half of the year principally related to the addition of our salesforce, and continued expansion of our marketing, market access and commercial capabilities and general and administrative support, and will remain consistent at that level in the second half of 2021. Accordingly, the timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Change in Fair Value of PIPE Warrant Liability (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
Change in fair value of PIPE Warrant liability	$ (2,396)	$ 2,648	$ (5,044)	(190)%

In May 2016, we issued PIPE Warrants, or the PIPE Warrants, in connection with a private placement financing and recorded the warrants as a liability. The PIPE Warrants are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in our Statement of Operations as a component of other income (expense).

In the three months ended March 31, 2021, we recorded an approximate non-cash loss of $2.4 million in our Statement of Operations attributable to the increase in the fair value of the PIPE Warrant liability that resulted from a higher stock price of $7.32 on March 31, 2021 compared to the stock price of $6.20 on December 31, 2020, an increase in our stock volatility rate and a shorter remaining term as the PIPE Warrants approach the scheduled expiration on May 16, 2021. The $2.4 million non-cash loss recognized in the first quarter of 2021, assuming no PIPE Warrants are exercised, will be fully reversed upon the May 16, 2021 expiration.

In the three months ended March 31, 2020, we recorded an approximate non-cash gain of $2.6 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that principally resulted from a lower stock price of $3.62 on March 31, 2020 compared to the stock price of $6.20 on December 31, 2019.

Interest Expense, net (in thousands)

	Three Months Ended March 31,		Comparison	
	2021	2020	$	%
Interest expense, net	$ (611)	$ (315)	$ (296)	94%

Interest expense, net increased by $0.3 million, or 94%, in the three months ended March 31, 2021 as compared to the same period in 2020. This increase was principally due to higher loan balances on a quarter-to-quarter basis under the 2020 Loan Amendment that was entered into with Hercules Capital Inc. and certain of its affiliates, or Hercules, on August 7, 2020. See “Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources — Hercules Loan Facility” below for a description of the 2020 Loan Amendment.

We anticipate that interest expense, net will increase in 2021 due to the $35.0 million loan balance as of March 31, 2021 and the extended interest-only period through September 30, 2022 pursuant to the 2020 Loan Amendment and 2021 Loan Amendment with Hercules.

Liquidity and Capital Resources

We have financed our operations to date primarily through private placements and public offerings of our common stock and preferred stock, license fees, milestone payments and research and development funding from strategic partners, and loan proceeds. As of March 31, 2021 we had cash and cash equivalents of approximately $121.4 million. See “Part II, Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources —Liquidity and Going Concern” below and Note 1 to the consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q for a further discussion of our liquidity. Currently, our funds are invested in a United States government money market fund.

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

	Three Months Ended March 31,	
	2021	2020
Net cash used in operating activities	$ (18,334)	$ (11,687)
Net cash provided by investing activities	—	7,748
Net cash provided by (used in) financing activities	77,987	(2,389)
Net increase (decrease) in cash and cash equivalents	$ 59,653	$ (6,328)

Our operating activities used cash of $18.3 million and $11.7 million in the three months ended March 31, 2021 and 2020, respectively. Cash used in operations was principally due to our net loss adjusted for non-cash items and changes in working capital.

Our investing activities provided cash of $7.7 million in the three months ended March 31, 2020 and none in the three months ended March 31, 2021, principally due to net changes in the maturities and purchases of marketable securities in the first quarter of 2020. We did not have any marketable securities in the first quarter of 2021.

Our financing activities provided cash of $78.0 million in the three months ended March 31, 2021 and used cash of $2.4 million in the three months ended March 31, 2020. In 2021, we raised approximately $78.0 million in funding, including approximately $51.6 million in net proceeds from the sale of approximately 6.9 million shares of our common stock in an underwritten public offering in March 2021, approximately $19.9 million in new loan funding pursuant to the 2020 Loan Amendment and 2021 Loan Amendment with Hercules, net of transaction costs, approximately $3.4 million in net proceeds from the sale of approximately 0.3 million shares of our common stock in March 2021 pursuant to our “at-the-market” sales agreement with SVB Leerink LLC, or SVB Leerink, which we refer to as the SVB Leerink Sales Agreement, and approximately $3.1 million in proceeds from the exercise of Offering Warrants. In 2020, we paid approximately $2.4 million in principal payments pursuant to our 2017 Loan Agreement with Hercules.

Hercules Loan Facility ($45 Million Loan Facility - $10 Million Committed Funding Remaining)

On May 28, 2010, the Company entered into a loan and security agreement, or the First Loan Agreement with Hercules. The First Loan Agreement was subsequently amended in March 2012, September 2014, May 2016 and amended and restated in December 2017, or the 2017 Loan Agreement. On August 7, 2020, we entered into a first amendment to the 2017 Loan Agreement or the 2020 Loan Amendment, to provide us, subject to certain terms and conditions, with additional term loans in an aggregate principal amount of up to $35.0 million, or the 2020 Loan Facility, to be used to repay in full the 2017 Loan Agreement and for general working capital purposes. The 2020 Loan Facility was made available to us in four tranches, the first of which, in the amount of $15.0 million, was made available to us immediately upon the closing of the 2020 Loan Amendment. We used the $15.0 million in proceeds of the first tranche as follows: approximately $9.7 million was used to repay the outstanding balance of the 2017 Loan Agreement in full, and approximately $5.3 million was used for general working capital purposes. In connection with the 2020 Loan Amendment, we incurred approximately $0.3 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2020 Loan Amendment was accounted for as a loan modification in accordance with ASC 470-50.

The remaining $20.0 million of term loans available to us under the 2020 Loan Facility subject to, among other terms and conditions, the achievement of the following milestones: (i) Tranche Two in the amount of $10.0 million, would be available through June 30, 2021 upon achieving Performance Milestone I for FDA approval of FOTIVDA, (ii) the third tranche, or Tranche Three, in the amount of $5.0 million, would be available from July 1, 2021 through January 31, 2022 if we achieve $20.0 million in net product revenues from sales of FOTIVDA, following FDA approval, by no later than December 31, 2021, or Performance Milestone II, and (iii) the fourth tranche, or Tranche Four, in the amount of $5.0 million, would be available through June 30, 2022 if we achieve both Performance Milestone I and Performance Milestone II, and if Hercules consents to the advancement of Tranche Four.

The 2020 Loan Amendment also amended the 2017 Loan Agreement by: (i) extending maturity of the loans from July 1, 2021 until September 1, 2023, which is extendable to September 1, 2024 upon our option if the Tranche Three funding has occurred, (ii) providing for an interest-only period beginning on the closing date of 2020 Loan Amendment and ending September 30, 2021, which

period may be extended through September 30, 2022 provided we achieved Performance Milestone I, and further extendable through March 31, 2023 if the Tranche Three funding has occurred, and (iii) revising the interest rate to the greater of 9.65% and an amount equal to 9.65% plus the prime rate minus 3.25% (subject to a 15% cap). Principal payments are scheduled to commence on October 1, 2021, at the earliest, as described above. The interest rate as of March 31, 2021 was 9.65%.

Pursuant to the terms of the Loan Agreement, principal will be repaid in equal monthly installments following the conclusion of the interest-only period. We may prepay all of the outstanding principal and accrued interest under the Loan Agreement, subject to a prepayment charge up to 3.0% in the first year following the closing of the 2020 Loan Amendment, decreasing to 2.0% in year two and 1.0% in year three. We are obligated to make an end-of-term payment of (i) 6.95% of the aggregate amount of loan funding received under the Loan Agreement on the earlier of the maturity of the loans or the date on which we prepay the outstanding loan balance in full, and (ii) an approximate $0.8 million payment due on the earlier of July 1, 2021 or the date on which we prepay the outstanding loan balance in full.

The Loan Agreement includes (i) a financial covenant that we maintain minimum unrestricted cash positions of $10.0 million through the date the Second Tranche funding is received, $15.0 million through the date the Third Tranche funding is received and $10.0 million thereafter through the maturity of the Loan Agreement, and (ii) an operating covenant that we achieve greater than or equal to 75% of our forecasted net product revenues from our sales of tivozanib over a 6-month trailing period, as defined and measured on a monthly basis, commencing upon the earlier to occur of (x) the Third Tranche funding and (y) the month of April 2022. The Loan Agreement also includes various other affirmative and negative covenants, including covenants to deliver certain financial reports; to maintain insurance coverage; and to refrain from transferring assets, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, and suffering a change in control, in each case subject to certain exceptions.

On February 1, 2021, we entered into the 2021 Loan Amendment. The 2021 Loan Amendment increased the aggregate principal amount of loans available under the 2020 Loan Facility from up to $35.0 million to up to $45.0 million following FDA approval of FOTIVDA. The 2021 Loan Amendment also (i) increased Tranche Two funding upon achieving Performance Milestone I from $10.0 million to $20.0 million, (ii) increased the amount of net product revenues from sales of FOTIVDA required for us to achieve Performance Milestone II from $20.0 million to $35.0 million, and changed the deadline for achieving Performance Milestone II from December 31, 2021 to April 1, 2022, and (iii) increased the amount of unrestricted cash required for us to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million. In connection with the 2021 Loan Amendment, we incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount.

On March 11, 2021, we completed the $20.0 million drawdown of Tranche Two funding under the 2021 Loan Amendment that was made available in connection with the achievement of Performance Milestone I upon FDA approval of FOTIVDA on March 10, 2021. The achievement of Performance Milestone I extended the interest-only period by twelve months from September 30, 2021 to September 30, 2022 and increased the amount of unrestricted cash required for us to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million.

As of March 31, 2021, the total principal balance was $35.0 million, principal payments are scheduled to commence on October 1, 2022 and the corresponding end-of-term payments under the 2020 Loan Facility, in the aggregate amount of approximately $2.4 million, are due upon the current loan maturity date of September 1, 2023. The unamortized discount to be recognized over the remainder of the loan period was approximately $2.6 million and $1.2 million as of March 31, 2021 and December 31, 2020, respectively. Per the 2017 Loan Agreement, the end-of-term payment of approximately $0.8 million continues to be due on July 1, 2021.

Obligations under the Loan Agreement are secured by substantially all of our assets, excluding intellectual property. The Loan Agreement provides that certain events shall constitute a default by us, including failure by us to pay amounts under the Loan Agreement when due; breach or default in the performance of any covenant under the Loan Agreement by us, subject to certain cure periods; our insolvency and certain other bankruptcy proceedings involving us; our default of obligations involving indebtedness in excess of $500,000; and the occurrence of an event or circumstance that would have a material adverse effect upon our business.

We have determined that the risk of subjective acceleration under the material adverse events clause included in the Loan Agreement is remote and, therefore, have classified the outstanding principal amount in long-term liabilities based on the timing of scheduled principal payments. As of March 31, 2021, we are in compliance with all of the loan covenants and, through the date of this filing, the lenders have not asserted any events of default under the Loan Agreement. We do not believe that there has been a material adverse change as defined in the Loan Agreement.

Public Offering – March 2021

On March 26, 2021, we completed an underwritten public offering of 6,900,000 shares of our common stock, including the full exercise by the underwriters of their option to purchase an additional 900,000 shares, at the public offering price of $8.00 per share for gross proceeds of approximately $55.2 million. The net offering proceeds to us were approximately $51.6 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Public Offering – June 2020

On June 19, 2020, we completed an underwritten public offering of 9,725,000 shares of our common stock, including the partial exercise by the underwriters of their option to purchase an additional 1,225,000 shares, at the public offering price of $5.25 per share for gross proceeds of approximately $51.1 million. Three stockholders each beneficially holding more than 5% of our voting securities, including an entity affiliated with New Enterprise Associates and two other stockholders purchased an aggregate of 4,503,571 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of our voting securities. The net offering proceeds to us were approximately $47.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Sales Agreement with SVB Leerink ($22 Million Availability Future Stock Sales)

In February 2018, we entered into the SVB Leerink Sales Agreement with SVB Leerink pursuant to which we may issue and sell shares of our common stock from time to time up to an aggregate amount of $50 million, at our option, through SVB Leerink as our sales agent, with any sales of common stock through SVB Leerink being made by any method that is deemed an "at-the-market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or in other transactions. Any such shares of common stock will be sold pursuant to a prospectus supplement filed under the 2020 Shelf, as defined below. We agreed to pay SVB Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the SVB Leerink Sales Agreement. We sold 470,777 shares, 1,251,555 shares, 1,070,175 shares and 330,688 shares pursuant to the SVB Leerink Sales Agreement, resulting in approximate proceeds net of commissions of $10.3 million, $7.5 million, $5.9 million and $3.4 million in the fourth quarter of 2018, February 2019, November 2020 and March 2021, respectively. As of March 31, 2021, approximately $22.2 million was available for issuance in connection with future stock sales pursuant to the SVB Leerink Sales Agreement.

Universal Shelf Registration Statement

On November 9, 2020, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of up to $300.0 million of our common stock, preferred stock, debt securities, warrants and/or units, or the 2020 Shelf. The 2020 Shelf (File No. 333-249982) was declared effective by the SEC on November 18, 2020 and was filed to replace our then existing shelf registration statement, which was terminated. As of March 31, 2021, there was approximately $213.0 million available for future issuance of our common stock, preferred stock, debt securities, warrants and/or units.

Public Offering – April 2019 (Offering Warrant Expiration – April 8, 2021)

In April 2019, we completed an underwritten public offering of 2,173,913 shares of our common stock and warrants to purchase an aggregate of 2,500,000 shares of our common stock, which we refer to herein as the Offering Warrants, including warrants to purchase an aggregate of 326,086 shares of our common stock sold pursuant to the underwriter's partial exercise of its overallotment option, at the public offering price of $11.40 per share and $0.10 per warrant for gross proceeds of approximately $25.0 million. The Offering Warrants were immediately exercisable upon issuance at an exercise price of $12.50 per share, subject to adjustment in certain circumstances, and expired two years from the date of issuance on April 8, 2021. Any Offering Warrants that had not been exercised for cash prior to their expiration were to be automatically exercised via cashless exercise on the expiration date. The shares and warrants were issued separately and were separately transferable. An entity affiliated with New Enterprise Associates purchased 434,782 shares and warrants to purchase an aggregate of 434,782 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of our voting securities. The net offering proceeds to us were approximately $22.8 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

In March 2021, Offering Warrants exercisable for 247,391 shares of common stock had been exercised, for approximately $3.1 million in cash proceeds, and Offering Warrants exercisable for 2,252,609 shares of our common stock were outstanding as of March 31, 2021. On April 8, 2021, all of the remaining 2,252,609 Offering Warrants expired and no shares of our common stock were issued via automatic cashless exercises of unexercised warrants on the date of expiration as the $12.50 exercise price was greater than our closing stock price of $7.01 on April 8, 2021.

Private Placement / PIPE Warrants (PIPE Warrant Expiration - Scheduled on May 16, 2021)

In May 2016, we entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which we sold 1,764,242 units, at a price of $9.65 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of our common stock and a PIPE Warrant to purchase one share of our common stock. The PIPE Warrants have an exercise price of $10.00 per share and are exercisable in any manner at any time for a period of five years from the date of issuance. Certain of our directors and executive officers purchased an aggregate of 54,402 units in this offering at the same price as the other investors. The net offering proceeds to us were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by us. As of March 31, 2021, PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding, at an exercise price of $10.00 per share, with a scheduled expiration date of May 16, 2021.

Liquidity and Going Concern

We have devoted substantially all of our resources to our drug development efforts, comprised of research and development, manufacturing, conducting clinical trials for our product candidates, protecting our intellectual property and general and administrative functions relating to these operations. Our future success is dependent on our ability to commercialize FOTIVDA in the United States and develop our clinical stage assets and, ultimately, upon our ability to create shareholder value.

On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. We anticipate that we will continue to incur significant operating expenses for the foreseeable future as we commercialize FOTIVDA in the United States and continue our planned development activities for our clinical stage assets. Our future product revenues will depend upon the size of markets in which FOTIVDA, and any future products, have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payers and adequate market share for FOTIVDA and any future products in those markets. The likelihood of our long-term success must be considered in light of the expenses, difficulties and potential delays that may be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which we operate. Absent the realization of sufficient revenues from product sales to support our cost structure, we may never attain or sustain profitability. We may require substantial additional funding to advance our pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources.

During the three months ended March 31, 2021, we received approximately $78.0 million in equity and loan funding, including approximately $51.6 million in net proceeds from the sale of approximately 6.9 million shares of our common stock in an underwritten public offering in March 2021, approximately $19.9 million in new loan funding pursuant to the 2020 Loan Amendment and 2021 Loan Amendment with Hercules, net of transaction costs, approximately $3.4 million in net proceeds from the sale of approximately 0.3 million shares of our common stock in March 2021 pursuant to our SVB Leerink Sales Agreement, and approximately $3.1 million in proceeds from the exercise of Offering Warrants.

We believe that our $121.4 million in cash and cash equivalents as of March 31, 2021, along with net product revenues from the commercial launch of FOTIVDA in the United States, would enable us to maintain our current operations for a period of at least 12 months following the filing of this Quarterly Form-10Q.

In 2021, we anticipate commercial operating expenses will be approximately $40.0 million, gross margins will be in the mid-to-high 80th percentile, research and development expenses will be approximately $40.0 million in support of our existing pipeline plans, and general and administrative expenses will remain at the level incurred in the first quarter of this year.

However, there are numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, including, without limitation, risks related to our ability to generate product revenue from sales of FOTIVDA in the United States, which became commercially available in the United States on March 22, 2021. Accordingly, our future funding requirements may vary from our current expectations and will depend on many factors, including, but not limited to:

- the cost of commercialization activities of FOTIVDA in the United States and any of our product candidates that may be approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing FOTIVDA in the United States, our product candidates and any additional products we may successfully commercialize;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of the product candidates we pursue;

- the scope, progress, results and costs of researching and developing our product candidates, and of conducting preclinical and clinical trials;
- the timing of, and the costs involved in, completing our clinical trials and obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our Loan Agreement, or under any other agreements with third parties;
- the cost and outcome of any legal actions against us;
- the timing, receipt and amount of sales of, or royalties on, tivozanib and our future products, if any;
- general economic, industry and market conditions; and
- the impact of COVID-19 on our operations, business and prospects.

We may require substantial additional funding to continue to advance our pipeline of clinical stage assets. We may seek to sell additional equity or debt securities or obtain additional credit facilities. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock or through additional credit facilities, these securities and/or the loans under credit facilities could provide for rights senior to those of our common stock and could contain covenants that would restrict our operations. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. We also expect to seek additional funds through arrangements with collaborators, licensees or other third parties. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or product candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all. If we are unable to raise substantial additional funding to advance our pipeline of clinical stage assets, whether on terms that are acceptable to us, or at all or if we were to default under the Loan Agreement, and Hercules accelerated the then remaining principal payments and fees due under the loan, then we may be required to:

- delay, limit, reduce or terminate our clinical trials or other development activities for one or more of our product candidates; and/or
- delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, if approved.

Contractual Obligations and Commitments

There have been no additional material changes to our contractual obligations and commitments outside the ordinary course of business from those disclosed in our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 16, 2021, except as discussed below.

On March 11, 2021, we completed the $20.0 million drawdown of Tranche Two funding under the 2021 Loan Amendment with Hercules that was made available in connection with the achievement of Performance Milestone I upon FDA approval of FOTIVDA on March 10, 2021. The achievement of Performance Milestone I extended the interest-only period by twelve months from September 30, 2021 to September 30, 2022. For more information, see “Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources —Hercules Loan Facility” below, as well as Note 6, “—Hercules Loan Facility” of the Notes to our consolidated financial statements, each included elsewhere in this Quarterly Report on Form 10-Q.

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 applicable SEC rules.

Item 4. Controls and Procedures.

Our management, with the participation of our President and Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of March 31, 2021. The term "disclosure controls and procedures" means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our President and Chief Executive Officer and Chief Financial Officer concluded that as of March 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, during the quarter ended March 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

From time to time, we may be subject to legal proceedings and claims in the ordinary course of business. As of the date of filing this Quarterly Report on Form 10-Q, there are no outstanding legal proceedings against us or our current officers or directors.

Item 1A. Risk Factors

You should carefully consider the risks described below in addition to the other information set forth in this Quarterly Report on Form 10-Q, including the Management's Discussion and Analysis of Financial Condition and Results of Operations section and the consolidated financial statements and related notes. These risks, some of which have occurred and any of which may occur in the future, can have a material adverse effect on our business, financial condition, results of operations or the price of our publicly traded securities. The risks described below are not the only risks we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial, may occur or become material in the future and adversely affect our business, reputation, financial condition, results of operations or the price of our publicly traded securities. Therefore, historical operating results, financial and business performance, events and trends are often not a reliable indicator of future operating results, financial and business performance, events or trends. If any of the following risks occurs, our business, financial condition, and results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant operating losses since inception and anticipate that we will continue to incur significant operating expenses for the foreseeable future. It is uncertain if we will ever achieve or sustain profitability.

We have a history of incurring operating losses and as of March 31, 2021, we had an accumulated deficit of $643.3 million. To date, we have not generated significant revenues from the sale of products. Our operating losses have resulted principally from costs incurred in our discovery and development activities. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. We anticipate that we will continue to incur significant operating expenses for the foreseeable future as we commercialize FOTIVDA in the United States and continue our planned development activities for our clinical stage assets. Our future product revenues will depend upon the size of markets in which FOTIVDA, and any future products, have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payers and adequate market share for FOTIVDA and any future products in those markets. The likelihood of our long-term success must be considered in light of the expenses, difficulties and potential delays to be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which we operate.

If we do not effectively manufacture, market and sell FOTIVDA in the United States and if we do not successfully develop, obtain and maintain regulatory approval for our existing and future pipeline of product candidates we may never generate sufficient revenues from product sales to support our cost structure in order to attain or sustain profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We may require substantial additional funding to advance our pipeline of clinical stage assets, and a failure to obtain this necessary capital when needed would force us to delay, limit, reduce or terminate our research, product development or commercialization efforts.

We believe that our $121.4 million in cash and cash equivalents as of March 31, 2021, along with net product revenues from the commercial launch of FOTIVDA in the United States, would enable us to maintain our current operations for a period of at least 12 months following the filing of this Quarterly Report on Form10-Q.

However, there are numerous risks and uncertainties associated with the research, development and commercialization of pharmaceutical products including, without limitation, risks related to our ability to generate product revenue from sales of FOTIVDA in the United States, which became commercially available in the United States on March 22, 2021. Accordingly, our future capital requirements may vary from our current expectations and depend on many factors, including but not limited to:

- the cost of commercialization activities of FOTIVDA in the United States and any of our product candidates that may be approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing FOTIVDA in the United States, our product candidates and any additional products we may successfully commercialize;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the number of product candidates we pursue as well as the development needs and opportunities for each product candidate;
- the scope, progress, results and costs of researching and developing our product candidates and of conducting preclinical and clinical trials;
- the timing of, and the costs involved in, completing our clinical trials and obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our Loan Agreement, or under any other agreements with third parties;
- the cost and outcome of any legal actions against us;
- the timing, receipt and amount of sales of, or royalties on, tivozanib and our future products, if any;
- general economic, industry and market conditions; and
- the impact of COVID-19 on our operations, business and prospects.

We may require substantial additional funding to advance our pipeline of clinical stage assets. We may seek to sell additional equity or debt securities or obtain additional credit facilities. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock or through additional credit facilities, these securities and/or the loans under credit facilities could provide for rights senior to those of our common stock and could contain covenants that would restrict our operations. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. For example, we may never achieve the milestones specified in the Loan Agreement that would allow us to access the remaining $10.0 million in available credit. We also expect to seek additional funds through arrangements with collaborators, licensees or other third parties. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or product candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all.

If we are unable to raise substantial additional funding to advance our pipeline of clinical stage assets, whether on terms that are acceptable to us, or at all, or we were to default under the Loan Agreement and Hercules accelerates the then remaining principal payments and fees due under the Loan Agreement, then we may be required to:

- delay, limit, reduce or terminate our clinical trials or other development activities for one or more of our product candidates; and/or
- delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, if approved.

Failure to comply with the covenants or payment obligations under the Loan Agreement could result in an event of default, which could materially and adversely affect our business and our financial condition.

The Loan Agreement includes certain financial and operational covenants and provide for certain occurrences that constitute events of default. Certain of those covenants may be out of our control, such as failure to achieve net product revenue at a certain percentage of projected net product revenue. Potential events of default also include circumstances occurring that have a material adverse effect on our business, our insolvency or bankruptcy, or default on our other obligations or agreements. If we fail to make payments when due, breach any operational covenant or have any event of default, Hercules could require us to immediately repay all outstanding principal and accrued interest on the loan, plus a prepayment charge, which could have a material adverse effect on our business and financial condition.

We have only recently transitioned from a development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Other than the marketing approvals for FOTIVDA received by our partner EUSA and the FDA marketing approval for FOTIVDA received in the United States in March 2021, all of our product candidates are in the development stage. We have not yet demonstrated our ability to manufacture a commercial scale medicine, or arrange for a third-party to do so on our behalf, or conduct significant sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had more experience commercializing our product candidates. In addition, as a newly commercial stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To be profitable, we will need to successfully transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Risks Related to Development and Commercialization of Our Product Candidates

In the near term, we are substantially dependent on the success of FOTIVDA (tivozanib). If we are unable to successfully commercialize FOTIVDA or maintain marketing approval for FOTIVDA in its approved indication, or if we are unable to complete planned or ongoing clinical development of tivozanib to obtain marketing approval for tivozanib in other indications, either alone or with our collaborators, or if we experience significant delays in doing so, our business could be substantially harmed.

Our prospects are substantially dependent on our ability to successfully commercialize FOTIVDA in the United States and maintain marketing approval for FOTIVDA in the United States, or through EUSA, in those countries outside the United States where FOTIVDA is currently approved. We are also dependent on the success of tivozanib in clinical development and our ability to obtain additional marketing approvals for tivozanib in one or more other indications.

The success of FOTIVDA will depend on a number of factors, including the following:

- our ability to successfully commercially launch FOTIVDA in the United States;
- commercial acceptance by patients, the medical community and third-party payors;
- our ability to gain access to customers during the COVID-19 pandemic;
- our ability to successfully enroll and complete clinical trials of tivozanib, including the DEDUCTIVE trial and the TiNivo-2 trial;
- a continued acceptable safety, tolerability and efficacy profile that is satisfactory to applicable regulatory authorities following any marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities such as the FDA;
- the performance of the contract research organizations, or CROs, we have hired to manage our clinical studies, as well as that of our collaborators and other third-party contractors;
- the extent of any future post-marketing approval commitments to applicable regulatory authorities;
- maintenance of existing or establishment of new supply arrangements with third-party raw materials suppliers and manufacturers including with respect to the supply of active pharmaceutical ingredient for tivozanib and finished drug product that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with KKC;
- protection of our rights in our intellectual property portfolio, including our ability to maintain our license agreement with KKC; and
- our ability to compete with other therapies.

Many of these factors are beyond our control. If we are unable to successfully commercialize FOTIVDA in the United States or to develop or receive marketing approval for tivozanib in other indications, on our own or with our collaborators, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

FOTIVDA, or any one of our product candidates that may receive marketing approval in the future, may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for FOTIVDA or any one of our product candidates may be smaller than our estimates.

Despite the recent FDA marketing approval of FOTIVDA in the United States, FOTIVDA, or any one of our product candidates that may be approved in the future by the appropriate regulatory authorities for marketing and sale, may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. There are already a number of therapies on the market competitive to tivozanib, as well as our other product candidates, in indications we intend to target.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. In light of the COVID-19 pandemic, we designed our strategic commercial approach for FOTIVDA to be flexible by building remote as well as in-person customer engagement capabilities in preparation for commercialization. However, it is uncertain whether obstacles and changes to standard sales and marketing practices resulting from the COVID-19 pandemic, including the shift from in-person to telephonic and virtual interactions with healthcare professionals, could negatively impact our commercialization efforts.

If FOTIVDA, or any of our product candidates that may be approved for marketing and sale in the future, does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of FOTIVDA, or any of our product candidates that may be approved for marketing and sale in the future, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the advantages of the product compared to competitive therapies;
- the number of competitors approved for similar uses;
- our ability to gain access to customers during the COVID-19 pandemic;
- the relative promotional effort and success of us as compared with our competitors;
- the prevalence and severity of any side effects;
- how the product is positioned in physician treatment guidelines and pathways;
- our ability to offer the product for sale at competitive prices;
- the product’s tolerability, convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including use restrictions, contained in the product’s approved labeling;
- the strength of sales, marketing and distribution support;
- the timing of market introduction of our approved products as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- potential product liability claims;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

In addition, the potential market opportunities for FOTIVDA and our product candidates are difficult to estimate precisely. Our estimates of the potential market opportunities are predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidate could be smaller than our estimates of the potential market opportunities.

In addition to our dependence on the success of FOTIVDA, we depend heavily on the success of our clinical stage assets, including tivozanib (in other indications), ficlatuzumab and AV-380. Preclinical studies and clinical trials of our product candidates may not be successful. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize our product candidates, either alone or with a collaborator, or if we experience significant delays in doing so, our business will be materially harmed.

We and any collaborators, including our partners and sublicensees, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. We and our collaborators must complete extensive preclinical development and clinical trials that demonstrate the safety and efficacy of our product candidates in humans before we can obtain these approvals.

We depend heavily on the success of our clinical stage assets and our clinical trials may not be successful. For instance, we have previously reported promising early clinical data on ficlatuzumab in HNSCC and we expect to receive top line data from the Phase 2 HNSCC Trial in the middle of 2021. If the results of this clinical trial are unfavorable, this would set us back. Further, we have initiated manufacturing of the clinical supply for a potential phase 3 clinical trial of ficlatuzumab and our investment may be lost if we were unable to move forward in a timely manner with a phase 3 clinical trial of ficlatuzumab.

Preclinical and clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all, particularly given that many of our clinical trial sites are research hospitals that have imposed restrictions on entry and other activity as a result of the COVID-19 pandemic. The preclinical and clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development. Moreover, we, or any collaborators, may experience any of a number of possible unforeseen adverse events in connection with clinical trials, many of which are beyond our control, including:

- we, or our collaborators, may fail to demonstrate efficacy in a clinical trial or across a broad population of patients;
- it is possible that even if one or more of our product candidates has a beneficial effect, that effect (a) will not be detected during preclinical or clinical evaluation or (b) may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials;
- we may fail to detect toxicity or intolerability of our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case;
- adverse events or undesirable side effects caused by, or other unexpected properties of, any product candidates that we may develop could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities;
- if any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective;
- regulators or institutional review boards may not authorize us, any collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results, including with respect to the safety, tolerability, efficacy or pharmacodynamic and pharmacokinetic profile of the product candidate;
- we, or any collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we, or any collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any collaborators, anticipate;

- our estimates of the patient populations available for study may be higher than actual patient numbers and result in our inability to sufficiently enroll our trials;

- the cost of planned clinical trials of our product candidates may be greater than we anticipate;

- our third-party contractors or those of any collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any collaborators in a timely manner or at all;

- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to increase the needed enrollment size for the clinical trial, extend the clinical trial's duration, or drop the patients from the final efficacy analysis for the clinical trial, which can negatively affect the statistical power of the results;

- our decision, or a decision by regulators or institutional review boards, that may require us to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;

- the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;

- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;

- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply;

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval; and

- constraints on our, or any collaborators', ability to conduct or complete clinical trials for our product candidates due to the COVID-19 pandemic, including slowdowns in patient enrollment, restrictions on patient monitoring at hospital clinical trial sites, closures of third-party facilities, and other disruptions to clinical trial activities.

Product development costs for us and our collaborators will increase if we experience delays in testing or pursuing marketing approvals, and we may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization. We do not know whether any trials will begin as planned, will need to be restructured or will be completed on schedule or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

If the commercial launch of FOTIVDA for which we recruited a sales force and established marketing, market access and medical affairs teams and distribution capabilities is not successful for any reason, we could incur substantial costs and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel.

To achieve commercial success for FOTIVDA, we have expended and anticipate that we will continue to expend significant resources to support our sales force, marketing, market access and medical affairs teams and distribution capabilities. There are risks involved with establishing our own sales, marketing, distribution, training and support capabilities. For example, recruiting and training sales and marketing personnel is expensive and time consuming and could delay our ability to focus on other priorities. If the commercial launch of FOTIVDA is not successful for any reason, this would be costly, and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel or terminate on favorable terms any agreements entered into with third parties to support our commercialization efforts.

Factors that may inhibit our efforts to commercialize FOTIVDA on our own include:

- our inability to train and retain adequate numbers of effective sales, marketing, training and support personnel;
- the inability of sales personnel to obtain access to physicians, including key opinion leaders, or to educate an adequate number of physicians of the benefits of FOTIVDA over alternative treatment options;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive or integrated product offerings; and
- unforeseen costs and expenses associated with establishing and maintaining an independent sales, marketing, training and support organization.

If our salesforce, marketing, market access and medical affairs teams and distribution capabilities fail, or are otherwise unsuccessful, it would materially adversely impact the commercial launch of FOTIVDA, impact our ability to generate revenue and harm our business.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the continued development and commercialization of FOTIVDA (tivozanib) is our primary focus, as part of our growth strategy, we are developing a pipeline of product candidates. These other product candidates will require additional, time-consuming and costly development efforts, by us or by our collaborators, prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace, or will be more effective than other commercially available alternatives.

We may not obtain additional marketing approvals for tivozanib in other indications or initial approval for our other product candidates.

We may not obtain additional marketing approvals for our product candidates. It is possible that the FDA or comparable foreign regulatory agencies may refuse to accept for substantive review any future application that we or a collaborator may submit to market and sell our product candidates, or that any such agency may conclude after review of our or our collaborator’s data that such application is insufficient to obtain marketing approval of our product candidate.

If the FDA or other comparable foreign regulatory agency does not accept or approve any future application to market and sell any of our product candidates, such regulators may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before they will reconsider our application. Depending on the extent of these or any other required trials or studies, approval of any application that we submit may be delayed by several years, or may require us or our collaborator to expend more resources than we or they have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA or other foreign regulatory agency to approve our applications for marketing and commercialization.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us or our collaborators from commercializing tivozanib in other indications or our product candidates and generating revenues related thereto. If any of these outcomes occur, we would not be eligible for certain milestone and royalty revenue under our partnership agreements, our collaborators could terminate our partnership agreements and we may be forced to abandon our development efforts for our product candidates, any of which could significantly harm our business.

Results of early clinical trials may not be predictive of results of later clinical trials, and interim results of clinical trials may not be predictive of the final results or the success of clinical trials.

The outcome of early clinical trials, such as our DEDUCTIVE trial and our ficlatuzumab trials in HNSCC, pancreatic cancer and AML, may not be predictive of the success of later clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we have, and could in the future, face similar setbacks. In addition, interim results and analyses of clinical trials do not necessarily predict the final results or the success of a trial once it is complete.

While the design of a clinical trial may help to establish whether its results will support approval of a product, flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates. For example, in June 2013, we suffered such a setback when the FDA issued a complete response letter, or the 2013 CRL, informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from the TIVO-1 trial, and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib did not adversely affect overall survival ("OS"). We then designed and initiated our TIVO-3 trial to address the FDA's concerns about the negative OS trend expressed in the 2013 CRL, which took time and resources and delayed our efforts to obtain marketing approval for tivozanib in the United States.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including differences in the size, type and geography of the patient populations, changes in trial procedures set forth in protocols, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the impact of the COVID-19 pandemic;
- the size and nature of the patient population;
- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment; and
- competing clinical trials.

In addition, participation in our clinical trials will be affected by clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied and the drug being provided as a control in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. For example, at the request of the FDA, we have updated the forms used to obtain consent from patients in ongoing and future trials with tivozanib to include information about the OS results from the TIVO-3 trial as well as the other tivozanib clinical trial OS results to date. These results may impact the interest of clinicians and patients in participating in future clinical trials with tivozanib.

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our ability to commence sales of and generate revenues from our product candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

We are conducting, and intend in the future to conduct, clinical trials for certain of our product candidates at sites outside the United States. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.

We are conducting, and intend in the future to conduct, one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice. The FDA must be able to validate the data from the trial through an onsite inspection if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, the FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

In addition, the conduct of clinical trials outside the United States could have a significant adverse impact on us or the trial results. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange rate fluctuations; and
- diminished protection of intellectual property in some countries.

Even if a product candidate receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability or that of any collaborators to market the product, and could cause regulatory authorities to take certain regulatory actions.

It is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. For example, despite the recent FDA marketing approval of FOTIVDA in the United States, we, or others, may discover that FOTIVDA is less effective or tolerable than previously believed. If, we, or others, discover that a product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any of our collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we, or any of our collaborators, may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any of our collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;

- physicians and patients may stop using our product; and
- our reputation may suffer.

Any of these events could harm our business and operations and could negatively impact our stock price.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of their potential for marketing approval and commercialization, as well as those that are most aligned with our strategic goals. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

We face substantial competition from existing approved products. Our competitors may also discover, develop or commercialize new competing products before, or more successfully, than we do.

The biotechnology and pharmaceutical industries are highly competitive, and our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of product candidates. Our core competitors include pharmaceutical and biotech organizations, as well as academic research institutions, clinical research laboratories and government agencies that are focusing on the research and development of small molecules and antibodies for cancer treatment. Many of our competitors have greater financial, technical and human resources than we do. Established competitors may invest heavily to discover and develop novel compounds that could make our product candidates obsolete.

For instance, there are several therapies in clinical development for RCC, HCC and HNSCC that may alter the competitive landscape for the treatment of these cancers. As such, it is difficult to predict how these changes will inform our perspective on the key competitors for our products in RCC, HCC and HNSCC in the future. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to obtain approval, to overcome price competition and to be commercially successful.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in favor of our competitors. Additionally, many competitors have greater experience in product discovery and development, obtaining FDA and other regulatory approvals and commercialization capabilities, which may provide them with a competitive advantage. If we are not able to compete effectively, our business will not grow and our financial condition and operations will suffer.

We believe that our ability to compete will depend on our ability to execute on the following objectives:

- design studies, execute on development plans and commercialize products that are competitive to other products in the market in terms of, among other things, safety, efficacy, convenience or price;
- obtain patent and/or other proprietary protection for our processes and product candidates;
- obtain required regulatory approvals;
- obtain favorable reimbursement, formulary and guideline status;
- collaborate with others in the design, development and commercialization of our products; and
- evaluate and pursue strategic business development and partnership opportunities for our programs.

FOTIVDA, or any other product candidate that we or our collaborators are able to commercialize, may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health care programs and private health insurers. For example, our European licensee for FOTIVDA, EUSA, is currently in the process of seeking reimbursement approval for FOTIVDA in many of the countries in which FOTIVDA has been approved. If coverage is not available, or reimbursement is limited, we, or any collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us or our collaborators to establish or maintain pricing sufficient to realize a sufficient return on our investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often time consuming and costly and may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any collaborators, to successfully commercialize any of our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably. These payors may not view our products, even if approved, as cost-effective, and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our products to be marketed on a competitive basis. Cost-control initiatives could cause us or our collaborators to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, such as FOTIVDA, and coverage may be more limited for FOTIVDA than the indication for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, for example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we, or third-parties, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we obtain regulatory approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall 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 a risk of product liability as a result of the commercialization of FOTIVDA and the clinical testing of our product candidates. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit the development or commercialization of our product candidates. Even a successful defense could require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased commercial demand for FOTIVDA, resulting in loss of revenue;
- delay or termination of our clinical trials, or the withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- the inability to develop or commercialize our product candidates;
- injury to our reputation and negative media attention; and
- a decline in our stock price.

Although we maintain general liability insurance and clinical trial liability insurance, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. Insurance coverage is becoming increasingly expensive. We increased our insurance coverage for the commercialization of FOTIVDA and we will need to increase our insurance coverage further if we commercialize any of our other products that receive marketing approval. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

Our internal computer systems or other company technology to collect and store information, or those of any third parties with which we contract, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber incidents by malicious third parties. Sensitive commercial and personal information also may be subject to security breaches in other contexts, related to personal devices or other technology or systems where this information can be collected, stored and used. Cyber incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber incidents could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, we face other kinds of risks related to our commercial and personal information, including lost or stolen devices or other systems (including paper records) that collect and store our personal and commercial information.

System failures, accidents, cyber incidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed or future trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. 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, our competitive position could be harmed and our product research, development and commercialization efforts could be delayed. We may in certain instances be required to provide notification to individuals or others in connection with the loss of their personal or commercial information. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Risks Related to Our Dependence on Third Parties

We rely on third parties, such as CROs, to conduct clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We, in consultation with our collaborators, where applicable, design the clinical trials for our product candidates, but we rely on CROs and other third parties to perform many of the functions in managing, monitoring and otherwise carrying out many of these trials. We compete with larger companies for the resources of these third parties. In addition, these third parties may be adversely affected by the COVID-19 pandemic.

Although we plan to continue to rely on these third parties to conduct our ongoing and any future clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA and foreign regulatory agencies require us to comply with regulations and standards, including good clinical practices, for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. The third parties on whom we rely generally may terminate their engagements with us at any time. If we are required to enter into alternative arrangements because of any such termination, the introduction of our product candidates to market could be delayed.

If these third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain, process and analyze is compromised for any reason or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may experience delays or may fail to meet regulatory requirements. If our clinical trials do not meet regulatory requirements or if these third parties need to be replaced, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates and our reputation could be harmed.

We rely on third-party manufacturers and third-party suppliers to produce, supply, store and transport our preclinical and clinical product candidate supplies, and we rely on third-parties to produce, store and distribute commercial supplies of FOTIVDA. Any failure by a third-party manufacturer or a third-party supplier to produce or provide supplies for us or to safely store product candidate supplies and commercial supplies of FOTIVDA may delay or impair our ability to complete our clinical trials or commercialize our product candidates.

We have relied upon third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing purposes and intend to continue to do so in the future. If we are unable to arrange for third-party manufacturing sources, or to do so on commercially reasonable terms, we may not be able to complete development of such product candidates or to market them.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third-party for regulatory compliance, quality assurance and safe-keeping of our product candidate supplies, the possibility of breach of the manufacturing agreement by the third-party because of factors beyond our control, failure of the third-party to accept orders for supply of drug substance or drug product and the possibility of termination or nonrenewal of the agreement by the third-party, based on its own business priorities, at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to current good manufacturing practices, or cGMPs. Any failure by our third-party manufacturers to comply with cGMPs or failure to scale-up manufacturing processes as needed, including any failure to safely transport and deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for action by the FDA to withdraw approvals for product candidates previously granted to us and for other regulatory action, including recall or seizure, fines, imposition of operating restrictions, total or partial suspension of production or injunctions.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies and commercial manufacturing. There are a small number of suppliers of raw and starting materials that we use to manufacture our product candidates. Such suppliers may not sell these materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers.

Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to the COVID-19 pandemic, the need to replace a third-party supplier or other factors could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates.

Because of the complex nature of many of our early stage compounds and product candidates, our manufacturers may not be able to manufacture such compounds and product candidates at a cost or quantity or in the timeframe necessary to develop and commercialize the related products. As our product development pipeline matures, we will have a greater need for commercial manufacturing capacity and we may be required to establish or access large-scale commercial manufacturing capabilities. In addition, we do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates and we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing, third parties with whom we currently work may need to increase their scale of production or we may need to secure alternate suppliers.

We rely on third parties to securely store product candidate supplies and commercial supplies of FOTIVDA. While we have sought to protect our product candidate supplies and commercial supplies of FOTIVDA through diversification of storage locations, there are times when such supplies may be placed in jeopardy due to unforeseen circumstances. If our product candidate supplies or commercial supplies of FOTIVDA were lost, destroyed or otherwise compromised, it would delay or impair our ability to complete clinical trials and commercialize FOTIVDA.

We rely on our licensee EUSA, over whom we have little control, for the sales, marketing and distribution efforts associated with the commercialization of FOTIVDA in certain European countries and any failure by EUSA to devote the necessary resources and attention to market and sell FOTIVDA effectively and successfully may materially impact our ability to generate revenue.

In December 2015, we entered into the EUSA Agreement, under which we granted to EUSA the exclusive, sublicensable right to develop, manufacture and commercialize FOTIVDA in the territories of Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa and Australasia for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye. We have limited contractual rights to force EUSA to invest significantly in the commercialization of FOTIVDA in jurisdictions covered by the EUSA Agreement. For instance, under the EUSA Agreement, EUSA is not required to opt into the data from the Tivo-3 trial to seek to expand the label for FOTIVDA to the relapsed or refractory RCC setting and, to date, has not chosen to do so. In the event that EUSA fails to adequately commercialize tivozanib because it lacks adequate financial or other resources, decides to focus on other initiatives or otherwise, our ability to successfully commercialize tivozanib in the applicable jurisdictions would be limited, which would adversely affect our business, financial condition, results of operations and prospects.

In addition, the EUSA Agreement may be terminated by either party upon prior written notice. If EUSA terminated the EUSA Agreement, we may not be able to secure an alternative distributor in the applicable territories on a timely basis or at all, in which case our ability to generate revenues from the sale of tivozanib, outside the United States would be materially harmed.

Further, while EUSA is working to secure reimbursement approval in and commercially launch FOTIVDA in additional EU countries, there is significant competition in the front-line RCC setting in the EU due to the approval of several immunotherapy combinations which have become a standard of care and impacted the market opportunity for monotherapy treatments. If EUSA is

unable to secure reimbursement approval in and commercially launch FOTIVDA in additional EU countries and does not seek to expand the label for FOTIVDA to the relapsed or refractory RCC setting, it may materially impact our ability to generate revenue from sales of FOTIVDA outside the United States.

We may not be successful in establishing or maintaining strategic partnerships to further the development of our therapeutic programs. Additionally, if any of our current or future strategic partners fails to perform its obligations or terminates the partnership, the development and commercialization of the product candidates under such agreement could be delayed or terminated. Such failures could have a material adverse effect on our operations and business.

Our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships with other biotechnology or pharmaceutical companies to support the development and commercialization of our product candidates. In these partnerships, we would expect our strategic partner to provide capabilities in research, development, marketing and sales, in addition to funding.

We face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any product candidates and programs because our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential.

If we are not able to establish and maintain strategic partnerships:

- the development of certain of our product candidates may be delayed or terminated;
- the internal cash expenditures needed to develop such product candidates would increase significantly, and we may not have the cash resources to develop such product candidates on our own; and
- we may have fewer resources with which to continue to operate our business.

Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us. Furthermore, we may not be able to maintain such strategic partnerships. If any current or future strategic partners do not devote sufficient time and resources to their arrangements with us, we may not realize the potential commercial benefits of the arrangement, and our results of operations may be adversely affected. For example, in March 2020, CANbridge advised us that it was evaluating alternative development plans for AV-203, which would delay the initiation of clinical trials of AV-203. Then, in March 2021, CANbridge exercised its right to terminate the CANbridge Agreement for convenience. Under the terms of the CANbridge Agreement, we expect the transfer of the AV-203 program to be complete in September 2021, which will delay the initiation of clinical trials of AV-203 even further. In addition, if the AV-203 program is not properly or timely transferred to us or data related to the AV-203 program is lost, destroyed or compromised, it would delay or hinder entirely our ability to advance the AV-203 program.

If any strategic partner were to breach or terminate its arrangements with us, the development and commercialization of the affected product candidate could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of the product candidate on our own. Our current partners and licensees can terminate their agreements with us under various conditions, including without cause, at which point they would no longer continue to develop our products. For example, in September 2020 Biodesix exercised its Opt-Out right under the Biodesix Agreement. As a result, Biodesix is not required to contribute to the future development costs of ficlatuzumab in exchange for a reduced economic interest in any future ficlatuzumab revenues.

Much of the potential revenue from any of our strategic partnerships will likely consist of contingent payments, such as development milestones and royalties payable on sales of any successfully developed drugs. Any such contingent revenue will depend upon our, and our strategic partners', ability to successfully develop, introduce, market and sell new drugs. In some cases, we are not involved in these processes, and we depend entirely on our strategic partners. Any of our strategic partners may fail to develop or effectively commercialize these drugs because it:

- decides not to devote the necessary resources due to internal constraints, such as limited personnel with the requisite scientific expertise, limited cash resources or specialized equipment limitations, or the belief that other product candidates may have a higher likelihood of obtaining regulatory approval or may potentially generate a greater return on investment;

- does not have sufficient resources necessary to carry the product candidate through clinical development, regulatory approval and commercialization; or
- cannot obtain the necessary regulatory approvals.

If one or more of our strategic partners fails to develop or effectively commercialize product candidates for any reason, we may not be able to replace the strategic partner with another partner to develop and commercialize a product candidate under the terms of the strategic partnership. We may also be unable to obtain, on terms acceptable to us, a license from such strategic partner to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

Risks Related to Our Intellectual Property Rights

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our product candidates, or the scope of our patent protection could be insufficiently broad, which could result in competition and a decrease in the potential market share for our product candidates.

We cannot be certain that patents will be issued or granted with respect to applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. For example, we have filed a patent application directed to our clinical protocol for using tivozanib to treat refractory cancers, including, following therapy with checkpoint inhibitors. It is possible that we may not successfully obtain a granted patent based upon this patent application. The scope of patent protection that the USPTO will grant with respect to the antibodies in our antibody product pipeline is also uncertain. It is possible that the USPTO will not allow broad antibody claims that cover closely related antibodies as well as the specific antibody. Upon receipt of FDA approval, competitors would be free to market antibodies almost identical to ours, including biosimilar antibodies, thereby decreasing our market share.

If we do not obtain patent term extensions under the Hatch-Waxman Act and similar non-U.S. legislation to extend the term of patents covering each of our product candidates, our business may be materially harmed.

Patents have a limited duration. The term of a U.S. patent, if granted from an application filed on or after June 8, 1995, is generally 20 years from its earliest U.S. non-provisional filing date. Even if patents covering our product candidates are obtained, once the patents expire, we may be open to competition from competitive medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned or in-licensed patent rights may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the circumstances, the term of our owned and in-licensed patent rights that cover our product candidates may be extended in the United States under the Hatch-Waxman Act, by Supplementary Protection Certificates, or SPCs, in certain European countries, and by similar legislation in other countries, for delays incurred when seeking marketing approval for a drug candidate. For example, the Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within the applicable deadline, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain a patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be materially reduced. For example, we have exclusive license rights to a first U.S. patent covering the tivozanib molecule and its therapeutic use, which is scheduled to expire in 2022, and a second U.S. patent covering a crystalline form of tivozanib, which is scheduled to expire in 2023. In view of the length of time tivozanib had been under regulatory review at the FDA, a patent term extension of up to five years may be available. Although we plan to apply for patent term extensions on each U.S. patent, only one patent may be extended, and, when appropriate, we will have to elect which patent is to be extended. If a five-year extension were to be granted, if applied to the first patent, the term could be extended to April of 2027, and if applied to the second patent, the term could be extended to November of 2028. However, the length of the extension could be less than we request, or no extension may be granted at all.

In addition, SPCs have been granted for the patent covering the tivozanib molecule in Belgium, Finland, France, Germany, Italy, the Netherlands, Norway, Poland, Portugal, Spain and Sweden, extending the term of the patents in each of these countries up to April 2027. An SPC has been granted for the patent covering the crystalline form of tivozanib in Ireland extending the term of that patent to October 2028. The remaining pending applications for SPCs on the patent covering the tivozanib molecule in Denmark and Great Britain may not be similarly granted, or may be granted for a shorter period than requested. If we are unable to obtain a patent term extension or the term of any such extension is less than we request, the period of time during which the patent rights covering tivozanib or its use can be enforced will be shortened, and our competitors may obtain approval to market a competing product sooner. As a result, our potential revenue from tivozanib could be materially reduced, causing material harm to our business.

Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in patent office proceedings, or in court.

If we or one of our strategic partners were to initiate legal proceedings against a third-party to enforce a patent covering one of our products, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. In addition, if we have a product approved by the FDA (for example, if the FDA approves our tivozanib product candidate), generic manufacturers could challenge the patents covering the approved product as part of the process of obtaining regulatory approval via an abbreviated new drug application, or ANDA. Grounds for a validity challenge could be an alleged failure to meet one or more statutory requirements for patentability, including, for example, lack of novelty, obviousness, lack of written description or non-enablement. In addition, patent validity challenges may, under certain circumstances, be based upon non-statutory obviousness-type double patenting, which, if successful, could result in a finding that the claims are invalid for obviousness-type double patenting or the loss of patent term, including a patent term adjustment granted by the USPTO, if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Additionally, third parties are able to challenge the validity of issued patents through administrative proceedings in the patent offices of certain countries, including the USPTO and the European Patent Office. Although we have conducted due diligence on patents we have exclusively in-licensed, and we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one of our products. Such a loss of patent protection could have a material adverse impact on our business.

Claims that our platform technologies, our products or the sale or use of our products infringe the patent rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.

We cannot guarantee that our platform technologies, our products or the use of our products, do not infringe third-party patents. Third parties might allege that we are infringing their patent rights or that we have misappropriated their trade secrets. Such third parties might resort to litigation against us. The basis of such litigation could be existing patents or patents that issue in the future.

It is also possible that we failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing, which is referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products.

With regard to ficlatuzumab, we are aware of one United States patent and its foreign counterparts that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. In the event that the owner of these patents were to bring an infringement action against us, we may have to argue that our product, its manufacture or use does not infringe a valid claim of the patent in question. Furthermore, if we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that, in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other patent rights of third parties, we may choose or be required to seek a license from a third-party and be required to pay license fees or royalties or both. These licenses may not be available on commercially acceptable terms, or at all. Even if we or our strategic partners were able to

obtain a license, the rights may be non-exclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time-consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business.

Unfavorable outcomes in an intellectual property litigation could limit our research and development activities and/or our ability to commercialize certain products.

If third parties successfully assert intellectual property rights against us, we might be barred from using aspects of our technology platform, or barred from developing and commercializing related products. Prohibitions against using specified technologies, or prohibitions against commercializing specified products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations of patent infringement or misappropriation of trade secrets, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in any litigation, including intellectual property litigation. There can be no assurance that we would prevail in any intellectual property litigation, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the patent owner in order to continue our research and development programs or our partnerships or to market our products. It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. This could limit our research and development activities, our ability to commercialize specified products, or both.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, in-license needed technology or enter into strategic partnerships that would help us bring our product candidates to market.

In addition, any future patent litigation, interference or other administrative proceedings will result in additional expense and distraction of our personnel. An adverse outcome in such litigation or proceedings may expose us or our strategic partners to loss of our proprietary position, expose us to significant liabilities or require us to seek licenses that may not be available on commercially acceptable terms, if at all.

An intellectual property litigation could lead to unfavorable publicity that could harm our reputation and cause the market price of our common stock to decline.

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs or intellectual property could be diminished. In such event, the market price of our common stock may decline.

Tivozanib and AV-380 are protected by patents exclusively licensed from other companies or institutions. If the licensors terminate the licenses or fail to maintain or enforce the underlying patents, our competitive position would be harmed and our partnerships could be terminated.

Certain of our product candidates and out-licensing arrangements depend on patents and/or patent applications owned by other companies or institutions with which we have entered into intellectual property licenses. In particular, we hold exclusive licenses from KKC for tivozanib and from St. Vincent’s for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which we refer to as GDF15 and which we use in our AV-380 program. We may enter into additional license agreements as part of the development of our business in the future. Our licensors may not successfully prosecute certain patent applications which we have licensed and on which our business depends or may prosecute them in a manner not in the best interests of our business. Even if patents issue from these applications, our licensors may fail to maintain these patents, may decide not to pursue litigation against third-party infringers, may fail to prove infringement or may fail to defend against counterclaims of patent invalidity or unenforceability. In addition, in spite of our best efforts, a licensor could claim that we have materially breached a license agreement and terminate the license, thereby removing our or our licensees’ ability to obtain regulatory approval for and to market any product covered by such license. If these in-licenses are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, identical products. In addition, the partners to which we have sublicensed certain rights under these licenses, such as EUSA, would likely have grounds for terminating our

partnerships if these licenses are terminated or the underlying patents are not maintained or enforced. This could have a material adverse effect on our results of operations, our competitive business position and our business prospects.

Confidentiality agreements with employees, consultants and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to patents, we rely on trade secrets, technical know-how and proprietary information concerning our business strategy in order to protect our competitive position. In the course of our research, development and business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to potential strategic partners. In addition, each of our employees and consultants are required to sign a confidentiality agreement upon joining our company. We take steps to protect our proprietary information, and we seek to carefully draft our confidentiality agreements to protect our proprietary interests. Nevertheless, there can be no guarantee that an employee, consultant or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures.

Trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information to competitors. Enforcing a claim that a third-party illegally obtained and is using any of our trade secrets is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than U.S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Our research and development strategic partners may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We rely significantly upon information technology, and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively and result in a material disruption of our product development programs.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our partners or fraudulently induce our employees or employees of our partners to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and computer viruses, cyber-attacks, or other system failures. Any system failure, accident or security breach that causes interruptions in our operations, for us or our partners, could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed clinical trials could result in delays in our regulatory approval efforts and we could incur significant increases in costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we may incur liabilities and the further development of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our partners occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Intellectual property rights may not 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 or antibodies 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.
- The term of patents that we own or have exclusively licensed may be insufficient to prevent competitors from introducing products that are competitive with our product candidates.
- If the licenses we have that relate to our product candidates are terminated by the licensors, we may be prevented from commercializing our product candidates.
- 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.
- Our pending patent applications might not lead to issued patents.
- Issued patents that we own or have exclusively licensed may not provide us with a competitive advantage; for example, our issued patents may not be broad enough to prevent the commercialization of products competitive with one or more of our product candidates, 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 or our strategic partners' existing or potential commercial markets.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, several events in the last decade have increased uncertainty with regard to our ability to obtain patents in the future and the value of patents once obtained. Among these, in September 2011, patent reform legislation passed by Congress was signed into law in the United States. The patent law introduced changes including a first-to-file system for determining which inventors may be entitled to receive patents, and post-grant challenges, such as inter-partes review and post-grant review proceedings that allow third parties to challenge newly issued patents. The burden of proof required for challenging a patent in these proceedings is lower than in district court litigation, and patents in the biopharmaceutical industry have been successfully challenged using these new post-grant challenges. In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in specified circumstances or weakening the rights of patent owners in specified situations. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could further weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Risks Related to the COVID-19 Pandemic

The COVID-19 pandemic has adversely disrupted, and is expected to continue to adversely disrupt our operations, including our ability to complete our ongoing clinical trials and may have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and has adversely impacted economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

We have enrolled and seek to enroll cancer patients in our ongoing clinical trials at sites located both in the United States and in Europe. The COVID-19 pandemic has delayed and may continue to delay or otherwise adversely affect these clinical development activities, including our ability to recruit and retain patients in our ongoing clinical trials, as a result of many factors, including:

- diversion of healthcare resources away from the conduct of our clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, availability of hospital staff supporting the conduct of our clinical trials and the reluctance of patients enrolled in our clinical trials to visit clinical trial sites;
- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples and other supplies used in our clinical trials;
- the impact of further limitations on travel that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by our employees, contractors or patients to clinical trial sites or the ability of employees at any of our contract manufacturing organizations, or CMOs, or CROs to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials, and limit the amount of clinical data we will be able to report;
- any future interruption of, or delays in receiving, supplies of clinical trial material from our contract manufacturing organizations or, in the case of combination trials, our study collaborators, due to staffing shortages, production slowdowns or stoppages or disruptions in delivery systems; and
- availability of future capacity at CMOs to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers elect or are required to divert attention or resources to the manufacture of other pharmaceutical products.

For example, some of the clinical trial sites for our DEDUCTIVE trial have suspended enrollment at times due to COVID-19 related hospital and governmental restrictions. Enrollment has occurred at a slower pace than initially forecasted prior to the onset of the pandemic, and we cannot guarantee the future pace of enrollment. In addition, in-person monitoring visits are currently on hold at certain of the clinical trial sites in our DEDUCTIVE trial and to the extent possible, due to the COVID-19 pandemic, monitoring is being conducted remotely. We do not yet know whether remote management of this function will prove to be sufficient. The extent of any adverse impact on our clinical trials will depend on numerous evolving factors that cannot be predicted with any level of certainty. In addition, in March 2020 we decided to discontinue the CyFi-2 trial due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, which had impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the ficlatuzumab clinical trial supply.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates or the regulatory review process could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital and have a material adverse effect on our financial results. In addition, our clinical trial patients who contract COVID-19 may have adverse health outcomes unrelated to their cancer that could impact the results of our clinical trials.

The COVID-19 pandemic continues to evolve and its ultimate scope, duration and effects are unknown. The extent of the impact of the disruptions to our business, preclinical studies, clinical trials and commercialization efforts as a result of the outbreak will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

The regulatory approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States, and by the EMA and comparable regulatory authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, especially if additional clinical trials are required. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. It also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may delay or preclude our obtaining marketing approval or prevent or limit commercial use.

In addition, the FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. In addition, a regulatory agency's varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. For example, in June 2013, the FDA issued the 2013 CRL informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from the TIVO-1 trial.

In addition, disruptions at the FDA and other agencies due to COVID-19 may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad and may limit our ability to generate revenue from product sales.

In order to market and sell our medicines in the EU and many other jurisdictions, we or our collaborators must obtain marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any particular market.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and any future collaborators and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we or any future collaborators fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we or any future collaborators fail to comply with applicable non-U.S. regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the EU, the United Kingdom withdrew from the EU, effective December 31, 2020. On December 24, 2020, the United Kingdom and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing any product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or the EU for any product candidates, which could significantly and materially harm our business.

We may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates, and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

We or our collaborators may seek orphan drug designations for other product candidates and may be unable to obtain such designations. Moreover, even if we do secure such designations and orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Further, even after an orphan drug is approved, the FDA can subsequently approve the same drug or biologic for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, to be more effective or to make a major contribution to patient care. Finally, orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Our recently approved product, FOTIVDA, and any product candidate for which we or our collaborators obtain marketing approval are subject to ongoing regulation and could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements.

Our recently approved product, FOTIVDA, and any product candidate for which we or our collaborators obtain marketing approval in the future will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy. For example, FDA approval of FOTIVDA is subject to limitations on the indicated uses for which FOTIVDA may be marketed, specifically the treatment of adults with relapsed or refractory advanced RCC who have progressed following two or more systemic therapies. Accordingly, we expect to continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approval for FOTIVDA withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

We and our collaborators must also comply with requirements concerning advertising and promotion for FOTIVDA or any of our product candidates for which we may obtain regulatory approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

Failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with healthcare providers, physicians and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of FOTIVDA and any product candidate for which we may obtain marketing approval in the future. Our arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute FOTIVDA and any products for which we may obtain marketing approval in the future. Restrictions under applicable federal and state healthcare laws and regulations include the federal Anti-Kickback Statute, the False Claims Act, Health Insurance Portability and Accountability Act of 1996, or HIPAA, and the Physician Payments Sunshine Act. There are also analogous state and foreign laws and regulations that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by third-party payors, including private insurers. Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and may require manufacturers to report information related to payments and other transfers of value to other healthcare providers and healthcare entities, or marketing expenditures.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from funded healthcare programs and the curtailment or restructuring of our operations. Any such penalties could adversely affect our financial results. We have implemented a corporate compliance program designed to ensure that we will market and sell FOTIVDA and any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect 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 impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell FOTIVDA or any product candidates for which we may obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we or any collaborators may receive for FOTIVDA or any product candidate for which we may obtain marketing approval in the future.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with the enactment of the Tax Cuts and Jobs Act of 2017, or TCJA, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court agreed to hear this case and a ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

Further, President Trump issued five executive orders intended to lower the costs of prescription drug products. Several of these orders are reflected in recently promulgated regulations, and one of these regulations is currently subject to a nationwide preliminary injunction. The Biden Administration has frozen certain of the previous administration's measures to reform drug prices, pending further review It remains to be seen how the Biden Administration will address this issue but, under Medicare Part D, the new administration may seek to establish a ceiling for the launch prices of all branded, biologic, and certain generic drugs by referencing the average price of these drugs in other developed countries. At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The Biden administration has agreed to delay for a year the implementation of one of President Trump's signature drug pricing policies. The policy at issue would have prevented drug makers and middlemen from negotiating rebates on prescription drugs. The prohibition was scheduled to go into effect in January 2022, but the Biden administration agreed to delay it until 2023.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological 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. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which

could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for FOTIVDA or our product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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 or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of FOTIVDA is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply, with additional laws and amendments being passed on a regular basis. As one example, the collection, use, disclosure, transfer or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which applies to all member states of the European Economic Area, or EEA. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data. The GDPR imposes significant obligations with respect to clinical trials conducted in the EEA. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU and otherwise across the world. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the California Consumer Privacy Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and Executive Orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, marketing or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Potential Growth

If we fail to attract and keep senior management, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management personnel. We are highly dependent upon our senior management, as well as others on our management team. The loss of services of employees and, in particular, of a member of management could delay or prevent our ability to successfully commercialize FOTIVDA in the United States, our ability to successfully maintain or enter into new licensing arrangements or collaborations, the successful development of our product candidates, the completion of our planned clinical trials or the commercialization of our product candidates. We do not carry "key person" insurance covering any members of our senior management. Our employment arrangements with all of these individuals are "at will," meaning they or we can terminate their service at any time.

We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to reward qualified individuals than we do. We may face challenges in retaining our existing senior management and key employees and recruiting new employees to join our company as our business needs change. In addition, the COVID-19 pandemic may negatively impact our ability to recruit and build out our organization as planned. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our future business plans.

Our employees or consultants may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee or consultant fraud or other misconduct. Misconduct by employees or consultants could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health-care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, marketing, sales 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 consultant 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 Conduct and Ethics, but it is not always possible to identify and deter employee or consultant misconduct, 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 impact on our business, including the imposition of significant fines or other sanctions.

In addition, during the course of our operations, our directors, executives, employees and consultants may have access to material nonpublic information regarding our business, our results of operations or potential transactions we are considering. Despite the adoption of an Insider Trading Policy, we may not be able to prevent a director, executive, employee or consultant from trading in our common stock on the basis of, or while having access to, material nonpublic information. If a director, executive, employee or consultant was to be investigated, or an action was to be brought against a director, executive, employee or consultant for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been, and is likely to be, highly volatile, and could fall below the price you paid. A significant decline in the value of our stock price could also result in securities class-action litigation against us.

The market price of our common stock has been, and is likely to continue to be, highly volatile and subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including:

- announcements relating to our product, FOTIVDA, including as it relates to commercial launch performance, sales and any future regulatory matters;
- new products, product candidates or new uses for existing products introduced or announced by our strategic partners, or our competitors, and the timing of these introductions or announcements;
- actual or anticipated results from and any delays in our clinical trials;
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock;
- the effect of the COVID-19 outbreak on the healthcare system and the economy generally and on our preclinical studies, clinical trials, commercial activities and other operations specifically;
- the results of regulatory reviews and other regulatory correspondence relating to our product, product candidates or our clinical trials;
- the results of our efforts to develop, acquire or in-license additional product candidates or products;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us of material developments in our business, financial condition, partnerships and/or operations;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- actual or anticipated changes in revenue, expense or earnings estimates, development timelines or recommendations by securities analysts; and
- general economic and market conditions on our industry and market conditions, 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.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

Periods of volatility in the market for a company's stock are often followed by litigation against the company. For example, following our failure to obtain FDA approval for tivozanib in 2013, we and certain of our former officers and directors were involved in several legal proceedings. Following our January 2019 announcement that the FDA did not recommend we file an NDA for tivozanib at that time, several lawsuits were filed against us, our directors, and certain of our current and former officers. See Part II, Item 1 of this Quarterly Report on Form 10-Q under the heading "Legal Proceedings." While the 2019 Class Action was dismissed, any litigation instituted against us in the future could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

We and our collaborators may not achieve development and commercialization goals in the estimated time frames that we publicly announce, which could have an adverse impact on our business and could cause our stock price to decline.

We set goals and make public statements regarding our expected timing for certain accomplishments, such as statements we have made about the initiation and completion of clinical trials, filing and approval of regulatory applications and other developments and milestones under our research and development programs and those of our partners and collaborators for tivozanib, ficlatuzumab, AV-380 and AV-203. The actual timing of these events can vary significantly due to a number of factors, including those discussed in "Part II, Item 1A. Risk Factors." As a result, there can be no assurance that our preclinical studies and clinical trials will advance or be completed in the time frames we expect or announce, that we will make regulatory submissions or receive regulatory approvals as planned, that we will be successful in our commercial launch or that we will be able to adhere to our currently anticipated schedule for the achievement of key milestones under any of our programs. If we fail to achieve one or more of the events described above as planned, our business could be materially adversely affected and the price of our common stock could decline.

Our management has broad discretion over our use of available cash and cash equivalents and might not spend our available cash and cash equivalents in ways that increase the value of your investment.

Our management has broad discretion on where and how to use our cash and cash equivalents and you will be relying on the judgment of our management regarding the application of our available cash and cash equivalents to fund our operations. Our management might not apply our cash and cash equivalents in ways that increase the value of your investment. We expect to use a substantial portion of our cash to fund existing and future research and development of our preclinical and clinical product candidates, with the balance, if any, to be used for working capital and other general corporate purposes, which may in the future include investments in, or acquisitions of, complementary businesses, joint ventures, partnerships, services or technologies. Our management might not be able to yield a significant return, if any, on any investment of this cash. You will not have the opportunity to influence our decisions on how to use our cash reserves.

If we fail to meet the requirements for continued listing on the Nasdaq Capital Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed on the Nasdaq Capital Market, or Nasdaq. We are required to meet specified requirements to maintain our listing on Nasdaq, including a minimum market value of listed securities of $35.0 million, a minimum bid price of $1.00 per share for our common stock and other continued listing requirements.

In the past we have, from time to time, received deficiency letters from Nasdaq as a consequence of our failure to satisfy such requirements. Although we have been able to regain compliance with the listing requirements within the manner and time periods prescribed by Nasdaq in the past, there can be no assurance that we will be able to maintain compliance with the Nasdaq continued listing requirements in the future or regain compliance with respect to any future deficiencies. If we fail to satisfy Nasdaq's continued listing requirements, we may transfer to the OTC Bulletin Board, which generally has lower financial requirements for initial listing, to avoid delisting. However, we may not be able to satisfy the initial listing requirements for the OTC Bulletin Board. Having our common stock trade on the OTC Bulletin Board could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

Fluctuations in our quarterly operating results could adversely affect the price of our common stock.

Our quarterly operating results may fluctuate significantly. Some of the factors that may cause our operating results to fluctuate on a period-to-period basis include:

- the level of net product revenues from the sales of FOTIVDA;
- the level of expenses incurred to commercialize FOTIVDA;
- the level of expenses incurred in connection with our clinical development programs, including development and manufacturing costs relating to our clinical development candidates;
- the implementation of restructuring and cost-savings strategies;
- the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement;
- costs associated with lawsuits against us or other litigation in which we may become involved, including the lawsuits described elsewhere in this Quarterly Report on Form 10-Q under “Part II, Item 1. – Legal Proceedings”;
- changes in our Loan Agreement, including the existence of any event of default that may accelerate then remaining principal payments and fees due thereunder;
- non-cash changes in fair value related to re-valuations of our outstanding warrant liability as a result of fluctuations in our stock price; and
- compliance with regulatory requirements.

Period-to-period comparisons of our historical and future financial results may not be meaningful, and investors should not rely on them as an indication of future performance. Our fluctuating results may fail to meet the expectations of securities analysts or investors. Our failure to meet these expectations may cause the price of our common stock to decline.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have been experiencing extreme volatility and disruptions in 2020 due to the COVID-19 pandemic and the government measures taken in response to the pandemic. We expect that rapid or extended periods of deterioration in credit and financial markets and confidence in economic conditions will continue. Our general business strategy may be adversely affected by external economic conditions and a volatile business environment or unpredictable and unstable market conditions. If the equity and credit markets are not favorable at any time we seek to raise capital, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers or other partners may not survive economically turbulent times, which could directly affect our ability to attain our operating goals on schedule and on budget.

As of March 31, 2021, we had approximately $121.4 million of cash and cash equivalents, consisting of cash on deposit with banks and in a U.S. government money market fund. As of the date of this report, we are not aware of any downgrades, material losses or other significant deterioration in the fair value of our cash equivalents or marketable securities. However, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents and marketable securities or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents and marketable securities owned by us.

Future sales of shares of our common stock, including shares issued upon the exercise of currently outstanding options and warrants, could negatively affect our stock price.

A substantial portion of our outstanding common stock can be traded without restriction at any time. Some of these shares are currently restricted as a result of securities laws, but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock. In addition, we have a significant number of shares that are subject to outstanding options and warrants. The exercise of these options or warrants and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

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

The trading market for our common stock may depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. A lack of research coverage may negatively impact the market price of our common stock. To the extent we do have analyst coverage, if one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Provisions of our certificate of incorporation, our by-laws or Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change in control of our company or changes in our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. These provisions include:

- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the ability of our board of directors to make, alter or repeal our by-laws; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that a stockholder could receive a premium for shares of our common stock held by a stockholder in an acquisition.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully respond to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

- responding to proxy contests and other actions by activist stockholders may be costly and time-consuming, and may disrupt our operations and divert the attention of management and our employees;
- perceived uncertainties as to the potential outcome of any proxy contest may result in our inability to consummate potential acquisitions, collaborations or in-licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals that have a specific agenda different from that of our management or other members of our board of directors are elected to our board of directors as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls, and requires our independent registered public accounting firm to attest to the effectiveness of our internal controls. Despite our efforts, we can provide no assurance as to our, or our independent registered public accounting firm's, conclusions with respect to the effectiveness of our internal control over financial reporting under Section 404. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we are unable to successfully remediate any material weaknesses in our internal control, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting and our stock price may decline as a result. We also could become subject to investigations by Nasdaq, the SEC or other regulatory authorities.

We do not expect to pay any cash dividends for the foreseeable future.

Our stockholders should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. In addition, the terms of the Loan Agreement preclude, and any future debt agreements may preclude us from, paying dividends. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the TCJA was enacted in 2017 and significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. In addition, as part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the CARES Act was enacted on March 27, 2020. Both contain numerous tax provisions.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act. We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA, the FFCR Act and the CARES Act and

other changes in tax laws on an investment in our common stock. Recent changes in tax law may adversely affect our business or financial condition.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2020, we had federal net operating loss carryforwards of $565.8 million, of which $502.6 million will, if not used, expire at various dates through 2037, and federal research and development tax credit carryforwards of $11.8 million, which will, if not used, expire at various dates through 2040. To the extent that they expire unused, these net operating loss and tax credit carryforwards will not be available to offset our future income tax liabilities. Federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such carryforwards is limited to 80% of our taxable income in the year in which such carryforwards are used.

In addition, under Section 382 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss and credit carryforwards to reduce its tax liability for post-change periods may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards is subject to an annual limitation under Section 382. We also may experience ownership changes in the future as a result of shifts in our stock ownership, some of which may be outside of our control. In addition, we have not conducted a detailed study to document whether our historical activities qualify to support the research and development credits currently claimed as a carryforward. A detailed study could result in adjustment to our research and development credit carryforwards. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, our use of those attributes to offset future income tax liabilities would be limited.

Item 6. Exhibits.

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated by Reference		Date of Filing	Exhibit Number	Filed Herewith
		Form	File Number			
10.1	First Amendment to Amended and Restated Loan and Security Agreement, dated as of August 7, 2020, by and among the registrant, Hercules Capital, Inc. and the other lenders named therein	10Q	001-34655	08/10/2020	10.1	
10.2†	Clinical Trial Collaboration and Supply Agreement, dated January 23, 2021, by and between the Registrant and Bristol-Myers Squibb Company					X
10.3†	Amendment No. 1 to Clinical Trial Collaboration and Supply Agreement, dated January 26, 2021, by and between the Registrant and Bristol-Myers Squibb Company					X
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.					X
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.					X
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.					X
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.					X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).					

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

Pursuant to the requirements 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.

AVEO PHARMACEUTICALS, INC.

Date: May 10, 2021

By: /s/ Erick Lucera

Erick Lucera
Chief Financial Officer and Principal Financial and Accounting Officer

Exhibit 10.2

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

EXECUTION VERSION
CONFIDENTIAL

CLINICAL TRIAL COLLABORATION AND SUPPLY AGREEMENT

This CLINICAL TRIAL COLLABORATION AND SUPPLY AGREEMENT (the "Agreement") is made and entered into effective as of the date signed by the last Party to sign below (the "Effective Date") by and between Aveo Pharmaceuticals, Inc., having a place of business at 30 Winter Street, Boston, MA 02108 (the "Recipient") and Bristol-Myers Squibb Company, having a place of business at Route 206 and Province Line Road, Princeton, New Jersey, USA 08543 ("BMS"). The Recipient and BMS are sometimes individually referred to in this Agreement as a "Party" and collectively as the "Parties."

PRELIMINARY STATEMENTS

A. The Recipient desires to conduct, and BMS desires to supply the BMS Study Drug (as defined below) for the conduct of, a Combined Therapy Clinical Trial (as defined below) in accordance with the Protocol (as defined below) therefor and in accordance with the terms of this Agreement.

B. The Parties desire to agree on various terms and conditions to govern the Parties' obligations in connection with the performance of the Combined Therapy Clinical Trial.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual promises and covenants contained herein, the Parties agree as follows:

ARTICLE 1

DEFINITIONS

The terms in this Agreement with initial letters capitalized, whether used in the singular or the plural, shall have the meaning set forth below or, if not listed below, the meaning designated in places throughout this Agreement.

"Adverse Event," ("AE") "Serious Adverse Event" ("SAE") and "Serious Adverse Drug Reaction" ("SADR") shall have the meanings provided to such terms in the International Conference on Harmonization ("ICH") guideline for industry on Clinical Safety Data Management (E2A, Definitions and Standards for Expedited Reporting).

"Affiliate" means, with respect to a particular Party, an entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such Party. As used in this definition, the term "controls" (with correlative meanings for the terms "controlled by" or "under common control with") means (a) that an entity owns, directly or indirectly, more than fifty percent (50%) of the voting stock of another entity, or (b) that an entity, person or group otherwise has the actual ability to control and direct the management of the entity, whether by contract or otherwise.

"Agreement" shall have the meaning set forth in the preamble to this Agreement, and includes the Appendices attached hereto, the PVA, Supply and Quality Documentation and any and all amendments of any of the foregoing hereafter signed by the Parties with reference to this Agreement and made part hereof.

"Applicable Law" means all applicable laws, rules and regulations (whether federal, state or local) that may be in effect from time to time, including current Good Clinical Practices (GCP), Good Laboratory Practices (GLP) and Good Manufacturing Practices (GMP).

"Arbitration Matter" means any disputed matter that relates to or arises out of the validity, interpretation or construction of, or the compliance with or breach of, this Agreement; provided that such disputed matter has been considered, but not resolved, by the Executive Officers as set forth in Section 13.3. For clarity, no Publication Dispute, or any matter requiring mutual agreement of both Parties shall be an Arbitration Matter.

"BMS Indemnitees" shall have the meaning set forth in Section 11.2.

"BMS Independent Patent Rights" means any Patent Rights Controlled by BMS (or its Affiliates) (a) as of the Effective Date or (b) during the Term the subject matter of which was conceived or first reduced to practice through activities other than those performed pursuant to this Agreement, in each case of (a) or (b) that Cover the use (whether alone or in combination with other agents), manufacture, formulation or composition of matter of the BMS Study Drug.

"BMS Regulatory Documentation" means any Regulatory Documentation pertaining to the BMS Study Drug that exists as of the Effective Date or that is created during the Term through efforts outside this Agreement.

"BMS Study Data" shall have the meaning set forth in Section 8.2.

"BMS Study Drug" means BMS's proprietary anti-PD-1 monoclonal antibody product known as Opdivo® (nivolumab).

"BMS Study Invention" means any Invention to the extent specifically relating to the BMS Study Drug (including compositions of matter or formulations of the BMS Study Drug and methods of use or manufacture of the BMS Study Drug as a monotherapy) and not relating to the Recipient Study Drug or the Combined Therapy.

"BMS Study Patent Rights" means any Patent Rights to the extent claiming any BMS Study Invention (and not claiming a Recipient Study Invention or Combined Therapy Invention). A patent containing claims claiming a BMS Study Invention and a Recipient Study Invention and/or a Combined Therapy Invention, shall be treated as a Combined Therapy Patent Right and not as a BMS Study Patent Right.

"BMS Technology" means all Technology Controlled by BMS (or its Affiliates) as of the Effective Date or during the Term created through efforts outside of this Agreement related to the BMS Study Drug or the Combined Therapy and necessary for the conduct of the Combined Therapy Clinical Trial. For clarity, BMS Technology does not include (a) Inventions, (b) Study Data, or (c) Combined Therapy Clinical Trial Regulatory Documentation.

"Breaching Party" shall have the meaning set forth in Section 12.2(a).

"Business Day" means a day other than Saturday, Sunday or any day on which commercial banks located in New York, NY or Boston, MA are authorized or obligated by Applicable Law to close.

"CDA" shall have the meaning set forth in Section 9.1.

"Clinical Hold" means that (a) the FDA has issued an order to a Party pursuant to 21 CFR §312.42 to delay a proposed clinical investigation or to suspend an ongoing clinical investigation of the Combined Therapy or such Party's Single Agent Study Drug in the United States or (b) a Regulatory Authority other than the FDA has issued an equivalent order to that set forth in (a) in any other country or group of countries.

"Combined Therapy" means a therapy using the Recipient Study Drug and the BMS Study Drug in combination with or without another agent.

"Combined Therapy Clinical Trial" means the human clinical trial in the Field using the Recipient Study Drug and the BMS Study Drug, which will be conducted under the Recipient's protocol (said protocol, as it may be amended from time to time in accordance with this Agreement, the "Protocol"), which is incorporated herein by reference. The draft Protocol as of the Effective Date is attached as Appendix A hereto.

"Combined Therapy IND" shall have the meaning set forth in Section 2.1(b).

"Combined Therapy Invention" means any Invention that is not a Recipient Study Invention or a BMS Study Invention.

"Combined Therapy Patent Right(s)" means any Patent Rights that Cover any Combined Therapy Invention or Combined Therapy Study Data, excluding BMS Independent Patent Rights and Recipient Independent Patent Rights.

"Combined Therapy Clinical Trial Regulatory Documentation" means any Regulatory Documentation to be submitted for the conduct of the Combined Therapy Clinical Trial, but excluding (a) any Recipient Regulatory Documentation and (b) any BMS Regulatory Documentation.

"Combined Therapy Study Data" shall have the meaning set forth in Section 8.3.

"Commercially Reasonable Efforts" means, with respect to a Party, [**].

"Confidential Information" shall have the meaning set forth in Section 9.1.

"Control" or "Controlled" means, with respect to particular information or intellectual property, that the applicable Party owns or has a license to such information or intellectual property and has the ability to grant a right, license or sublicense to the other Party as provided for herein without violating the terms of any agreement or other arrangement with any Third Party.

"Cover" means, with respect to a Patent Right, that, but for rights granted to a Person under such Patent Right, the practice by such Person of an invention described in such Patent Right would infringe a claim included in such Patent Right, or in the case of a Patent Right that is a patent application, would infringe a claim in such patent application if it were to issue as a patent. "Covered" or "Covering" shall have correlative meanings.

"CRO" means any Third Party contract research organization used to conduct the Combined Therapy Clinical Trial, including laboratories and Third Parties used to maintain the safety database from the Combined Therapy Clinical Trial, but, for clarity, excluding clinical trial sites and any Third Parties who are individuals.

"Cure Period" shall have the meaning set forth in Section 12.2(a).

"[**]" means [**].

"[**]" means [**].

"Date of First Receipt" means, with respect to a Party, the date on which any employee of such Party, its Affiliates or its Third Party subcontractors first becomes aware of safety-related information.

"Designated Clinical Contact" shall have the meaning set forth in Section 2.3. "Designated Supply Contact" shall have the meaning set forth in Section 4.7. "Dispute" shall have the meaning set forth in Section 13.3(b).

"Effective Date" shall have the meaning set forth in the preamble to this Agreement. [**] shall mean [**].

[**] Territory” means the countries listed in Appendix E.

“Executive Officers” means the Chief Executive Officer of the Recipient and the Head of Oncology Development of BMS (or their respective designees).

“FDA” means the United States Food and Drug Administration, or any successor agency having the same or similar authority.

“Field” means the diagnosis, prevention and treatment of any and all oncologic diseases and conditions in humans.

“Filing Party” shall have the meaning set forth in Section 6.1(c).

“Global Safety Database” means the database containing Adverse Events, Serious Adverse Events, Serious Adverse Drug Reactions and pregnancy reports for the Combined Therapy, and shall be the authoritative data source for regulatory reporting and responding to regulatory queries with respect to the Combined Therapy Clinical Trial.

“Good Clinical Practices” or “GCP” means, as to the United States and the European Union, applicable good clinical practices as in effect in the United States and the European Union, respectively, during the Term and, with respect to any other jurisdiction, clinical practices equivalent to good clinical practices as then in effect in the United States or the European Union.

“Good Laboratory Practices” or “GLP” means, as to the United States and the European Union, applicable good laboratory practices as in effect in the United States and the European Union, respectively, during the Term and, with respect to any other jurisdiction, laboratory practices equivalent to good laboratory practices as then in effect in the United States or the European Union.

“Good Manufacturing Practices” or “GMP” means, as to the United States and the European Union, applicable good manufacturing practices as in effect in the United States and the European Union, respectively, during the Term and, with respect to any other jurisdiction, manufacturing practices equivalent to good manufacturing practices as then in effect in the United States or the European Union.

“ICF” shall have the meaning set forth in Section 5.1(f).

“IND” means (a) an Investigational New Drug Application as defined in the United States Food, Drug and Cosmetic Act, as amended, and regulations promulgated thereunder, or any successor application or procedure required to initiate clinical testing of a drug in humans in the United States, (b) a counterpart of such an Investigational New Drug Application that is required in any other country before beginning clinical testing of a drug in humans in such country, including, for clarity, a “Clinical Trial Application” in the European Union, and (c) all supplements and amendments to any of the foregoing.

“Indemnify” shall have the meaning set forth in Section 11.1.

“Infringe” and “Infringement” means any alleged or threatened (in writing) infringement, or misappropriation by a Third Party, of any Patent Rights.

“Invention” means any invention or Technology, whether or not patentable, that is made, conceived, or first actually reduced to practice by, for or on behalf of a Party, or by, for or on behalf of the Parties together (including by a Third Party in the performance of the Combined Therapy Clinical Trial), (a) in relation to the Combined Therapy Clinical Trial to be conducted under this Agreement or (b) by the use of Study Data, but excluding in each case any Study Data.

“IRB” means an Investigational Review Board or Ethics Committee (or similar body in a given country).

[**] means [**]

[**] Territory" means the countries listed in Appendix D. "Licensee" shall have the meaning set forth in Section 13.10(b). "Losses" shall have the meaning set forth in Section 11.1.

"Manufacture" or "Manufacturing" means manufacturing, processing, formulating, packaging, labeling, holding (including storage), and quality control testing of a Single Agent Study Drug or the Combined Therapy, in each case so as to be suitable for use in the Combined Therapy Clinical Trial under Applicable Law.

"Material Safety Issue" means a Party's good faith belief that there is an unacceptable risk for harm in humans based upon: (a) pre-clinical safety data, including data from animal toxicology studies, or (b) the observation of Serious Adverse Events in humans after the Recipient Study Drug or the BMS Study Drug, either as a Single Agent Study Drug or in combination with another pharmaceutical agent (including as the Combined Therapy), has been administered to or taken by humans, such as during the Combined Therapy Clinical Trial.

"NDA" means (a) any new drug application or biologics license application filed with the FDA, or any successor application or procedure required to introduce a drug or biologic into commerce in the United States, (b) a counterpart of such a new drug application or biologics license application that is required in any other country before beginning the commercialization of a drug or a biologic in humans in such country, and (c) all supplements and amendments to any of the foregoing.

"Non-Breaching Party" shall have the meaning set forth in Section 12.2(a). "Officials" shall have the meaning set forth in Section 10.9.

"[**]" means [**].

"[**]" means [**].

"[**]" means [**].

"Operational Matters" shall have the meaning set forth in Section 5.1.

"Party" or "Parties" shall have the meaning set forth in the preamble to this Agreement.

"Patent Rights" means any (a) United States or foreign patents, (b) United States or foreign patent applications, including all provisional applications, substitutions, continuations, continuations-in-part, divisions, renewals, and all patents granted thereon, (c) United States or foreign patents-of-addition, reissues, reexaminations (including ex parte reexaminations, inter partes reviews, inter partes reexaminations, post grant reviews and supplemental examinations) and extensions or restorations by existing or future extension or restoration mechanisms, including supplementary protection certificates, patent term extensions, or the equivalents thereof, and (d) any other form of government-issued right substantially similar to any of the foregoing.

"Payment" shall have the meaning set forth in Section 10.9.

"Person" means any individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department or agency of a government.

"Personal Data" means any information relating to an identified or identifiable natural person. "POTV" shall have the meaning set forth in Section 9.6(a).

"Protocol" shall have the meaning set forth in the definition of Combined Therapy Clinical Trial. "Publication Dispute" shall have the meaning set forth in Section 9.5(b).

"PVA" shall have the meaning set forth in Section 2.2. "Quarter" means a calendar quarter.

“Recipient Indemnitees” shall have the meaning set forth in Section 11.1.

“Recipient Independent Patent Rights” means any Patent Rights Controlled by the Recipient or a Recipient Affiliate (a) as of the Effective Date or (b) during the Term the subject matter of which was conceived or first reduced to practice through activities other than those performed pursuant to this Agreement, in each case (a) and (b) that Cover the use (either alone or in combination with other agents), manufacture, formulation or composition of matter of the Recipient Study Drug.

“Recipient License Agreements” shall means (a) that certain License Agreement entered into as of [**], as amended from time to time and (b) that certain License Agreement entered into as of [**], as amended from time to time.

“Recipient Regulatory Documentation” means any Regulatory Documentation pertaining to the Recipient Study Drug that exists as of the Effective Date or that is created during the Term through efforts outside this Agreement.

“Recipient Study Data” shall have the meaning set forth in Section 8.2.

“Recipient Study Drug” means the Recipient’s proprietary small molecule vascular endothelial growth factor (“VEGF”) tyrosine kinase inhibitor (“TKI”) known as Fotivda® (tivozanib).

“Recipient Study Invention” means any Invention to the extent specifically relating to the Recipient Study Drug (including compositions of matter or formulations of the Recipient Study Drug and methods of use or manufacture of the Recipient Study Drug as a monotherapy) and not relating to the BMS Study Drug or the Combined Therapy.

“Recipient Study Patent Rights” means any Patent Rights to the extent claiming any Recipient Study Invention (and not claiming a BMS Study Invention or a Combined Therapy Invention). A patent containing claims claiming a Recipient Study Invention and a BMS Study Invention and/or a Combined Therapy Invention, shall be treated as a Combined Therapy Patent Right and not as a Recipient Study Patent Right.

“Recipient Technology” means all Technology Controlled by the Recipient or a Recipient Affiliate as of the Effective Date or during the Term created through efforts outside of this Agreement related to the Recipient Study Drug or the Combined Therapy. For clarity, Recipient Technology does not include (a) Inventions, (b) Study Data, or (c) Combined Therapy Clinical Trial Regulatory Documentation.

“Regulatory Approval” mean any and all approvals (including supplements, amendments, variations, label expansion, indication extensions, pre- and post-approvals, NDA or BLA approvals, and their foreign equivalents such as MAA approvals), licenses, registrations or authorizations (including marketing and labelling authorizations) of any national, supra-national (e.g., the European Union), regional, state or local Regulatory Authority, department, bureau, commission, council or other governmental entity, that are necessary for the commercial manufacture, commercial use, or sale of a product in a given jurisdiction.

“Regulatory Authority” means the FDA or any other governmental authority outside the United States (whether supranational, national, federal, provincial and/or local) that is the counterpart to the FDA, including the European Medicines Agency for the European Union.

“Regulatory Documentation” means, with respect to a Party’s Single Agent Study Drug, all submissions to Regulatory Authorities in connection with the development of such Single Agent Study Drug, as applicable, including all INDs and amendments thereto, NDAs and amendments thereto, drug master files, correspondence with regulatory agencies, periodic safety update reports, adverse event files, complaint files, inspection reports and manufacturing records, in each case together with all supporting documents (including documents that include clinical data). For clarity, Regulatory Documentation excludes documentation related to the commercial sale of a product in a given jurisdiction.

"Results" shall have the meaning set forth in Section 9.5(b).

"Right of Cross-Reference" means, with regard to a Party, allowing the applicable Regulatory Authority in a country to have access to relevant information (by cross-reference, incorporation by reference or otherwise) contained in Regulatory Documentation (and any data contained therein) filed with such Regulatory Authority with respect to a Party's Single Agent Study Drug (and, in the case of BMS, the Right to Cross-Reference the Combined Therapy IND), only to the extent necessary for the conduct of the Combined Therapy Clinical Trial in such country or as otherwise expressly permitted or required under this Agreement to enable a Party to exercise its rights or perform its obligations hereunder, and, except as to information contained in the Combined Therapy IND pertaining to the Combined Therapy, without the disclosure of such information to such Party.

"Safety Issue" means any information suggesting an emerging safety concern or possible change in the risk-benefit balance for the BMS Study Drug or the Recipient Study Drug, including information on a possible causal relationship between an Adverse Event and a drug, the relationship being unknown or incompletely documented previously.

"Safety Signal" means information arising from one or multiple sources, including observations and experiments, which suggests a new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action.

"Samples" means biological specimens collected from Combined Therapy Clinical Trial study subjects (including fresh and/or archived tumor samples, serum, peripheral blood mononuclear cells, plasma, and whole blood for RNA and DNA sample isolation).

"Shortage" shall have meaning set forth in Section 4.5.

"Single Agent Study Drug" or "Study Drug" means, with respect to (a) the Recipient, the Recipient Study Drug, as monotherapy, and (b) BMS, the BMS Study Drug, as monotherapy.

"Sponsor" means an applicant or holder of clinical studies applications/notifications. "Study Data" shall have the meaning set forth in Section 8.1.

"Sunshine Laws" shall have the meaning set forth in Section 9.6(c).

"Supply and Quality Documentation" shall have the meaning set forth in Section 4.3.

"Technology" means information, inventions, discoveries, trade secrets, knowledge, technology, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, specifications, data and results not generally known to the public (including biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data and know-how, including study designs and protocols), in all cases, whether or not patentable, in written, electronic or any other form now known or hereafter developed and materials, including Regulatory Documentation.

"Term" shall have the meaning set forth in Section 12.1.

"Territory" means the countries listed in Appendix C. [**].

"Third Party" means any Person or entity other than the Recipient and BMS and their respective Affiliates.

"Third Party Claim" shall have the meaning set forth in Section 11.1.

"Third Party License Payments" means any payments (e.g., upfront payments, milestones, royalties) due to any Third Party under license agreements or other written agreements granting rights to intellectual property owned or controlled by such Third Party to the extent that such rights are necessary for (a) the making, using or importing of a Party's Single Agent Study Drug for the conduct of the Combined Therapy Clinical Trial, or (b) the conduct of the Combined Therapy Clinical Trial.

"TP Study Costs" shall have the meaning set forth in Section 7.2.

ARTICLE 2

SCOPE

2.1 Scope.

(a) The Recipient will conduct the Combined Therapy Clinical Trial in accordance with the Protocol and the terms of this Agreement. The Recipient shall be solely responsible for the content of the Protocol; provided that: (i) the Recipient will notify BMS of any proposed amendments to the draft Protocol attached as Appendix A to this Agreement (or to the final Protocol initially approved by an IRB) and the Recipient will consider any comments provided by BMS regarding the proposed amendments, and (ii) any changes to the draft Protocol attached as Appendix A (or to the final Protocol initially approved by an IRB) that pertain to the administration of the BMS Study Drug must be reviewed and expressly approved by BMS in writing or the change may not be implemented. BMS shall have [**] from the date on which the Recipient provides the applicable Protocol amendment to BMS to approve or provide any comments to the Recipient concerning the proposed amendment.

(b) The Combined Therapy Clinical Trial shall be conducted under a combination IND, for which the Recipient will be the sponsor of record (the "Combined Therapy IND") and shall be conducted only in the Territory in the Field. The Recipient shall be the sole holder of all legal interests in the Combined Therapy IND; provided, however, that the Recipient may not grant any Third Party any Right of Cross-Reference with respect to any portion of the Combined Therapy IND pertaining to BMS's Single Agent Study Drug for use as monotherapy or for use in combination with any molecules, agents, antibodies or compounds other than the Recipient Study Drug.

(c) BMS will make available its current package insert for the BMS Study Drug in the Territory available to the Recipient and will provide any updates thereto at the same time as the same are made publicly available.

(d) If the Recipient and BMS agree that the Recipient will require access to the investigator's brochure for the BMS Study Drug in order for the site to conduct the Combined Therapy Clinical Trial, then (i) BMS will provide the current version of its Investigator Brochure to the Recipient promptly and (ii) will thereafter, until the conclusion of the Combined Therapy Clinical Trial, provide to the Recipient, upon reasonable request, the latest investigator's brochure for the BMS Study Drug or any amendments thereto in accordance with BMS's customary practices for same. The Recipient shall, and shall require that any clinical trial sites for the Combined Therapy Clinical Trial shall, use any such data provided pursuant to this Section 2.1(d) solely (A) to evaluate the safety and efficacy of the BMS Study Drug and the Combined Therapy for use in Combined Therapy Clinical Trial, (B) to meet any regulatory requirements pertaining to the conduct of the Combined Therapy Clinical Trial and (C) to enable the Recipient to draft and update as necessary the investigator's brochure for the Combined Therapy Clinical Trial. The Recipient will ensure that clinical trial sites for the Combined Therapy Clinical Trial are obligated to protect such information and disclosures as set forth in Article 9. The Recipient's right to use the investigator's brochure provided by BMS shall terminate upon the expiration or termination of the Combined Therapy Clinical Trial and shall not be used for purposes of conducting any other clinical studies.

(e) If requested in writing by the Recipient and agreed to by BMS (such consent not to be unreasonably withheld), BMS shall provide a Right of Cross-Reference as needed to its existing

Regulatory Documentation for BMS's Single Agent Study Drug for those countries in the Territory where the Combined Therapy Clinical Trial will be conducted solely as necessary to allow the Combined Therapy Clinical Trial to be conducted in an applicable country; provided that such Right of Cross-Reference shall terminate upon the expiration or termination of this Agreement and shall not be used for purposes of conducting any other clinical studies, except that, in the case of termination for a Material Safety Issue pursuant to Section 12.4, such Right of Cross-Reference shall remain in effect solely (i) to the extent necessary to permit the Recipient to comply with any outstanding obligations required by a Regulatory Authority and/or Applicable Law or (ii) as necessary to permit the Recipient to continue to dose subjects enrolled in the Combined Therapy Clinical Trial through completion of the Protocol if required by the applicable Regulatory Authority(ies) and/or Applicable Laws.

(f) If [**] is incorporated into the Protocol, the Recipient agrees to use the [**] perform such testing.

(g) The Recipient shall refer to the applicable BMS Study identification number in all Combined Therapy Clinical Trial reports, reports of Serious Adverse Events, BMS Study Drug requests, and all other material submissions or communications to BMS relating to the Protocol.

2.2 Adverse Event Reporting. The Parties shall use diligent efforts to define and finalize the processes the Parties shall employ to protect patients and promote their well-being in connection with the use of each Combined Therapy, and to execute a written Pharmacovigilance Agreement ("PVA") within [**] after the Effective Date of this Agreement or sooner as practicable and agreed to by the Parties, and prior to the first dosing of the first study patient in any new clinical trial subject to this Agreement. Such PVA shall (a) provide that Recipient shall hold and be responsible for the maintenance of the Global Safety Database for the Recipient Study Drug and that BMS shall hold and be responsible for the maintenance of the Global Safety Database for the BMS Study Drug, (b) provide that Recipient shall be responsible for the safety reporting for the Combined Therapy and shall lead all pharmacovigilance activities for the Combined Therapy, (c) permit Recipient to disclose or otherwise make available [**] information in the Global Safety Database applicable to the Recipient Study Drug, and (d) include mutually acceptable guidelines and procedures for the receipt, investigation, recordation, communication, and exchange (as between the Parties) of adverse event reports, pregnancy reports, and any other information concerning the safety of the Combined Therapy. Such guidelines and procedures shall be in accordance with, and enable the Parties and their Affiliates to fulfill, local and international regulatory reporting obligations to government authorities. Furthermore, such agreed procedures shall be consistent with relevant International Council for Harmonization (ICH) guidelines, except where said guidelines may conflict with existing local regulatory safety reporting requirements or Applicable Law, in which case local reporting requirements or Applicable Law shall prevail. In the event of a conflict between the terms this Agreement and the terms of the PVA, the PVA shall supersede to the extent related to pharmacovigilance matters associated with the Combined Therapy Clinical Trial and the terms of this Agreement control with respect to any other matters. In the event that this Agreement is terminated, the Parties agree to implement the necessary procedures and practices to ensure that any outstanding pharmacovigilance reporting obligations are fulfilled.

2.3 Clinical Study Designated Contact. Each Party will designate an employee within its organization (the "Designated Clinical Contact") who will coordinate and/or facilitate:

(a) the review of Protocol amendments submitted by the Recipient for BMS approval or comment and with whom comments thereon may be discussed;

(b) any BMS clinical and regulatory responsibilities and communications regarding the Combined Therapy Clinical Trial;

(c) internal BMS review of any document or regulatory communication and the provision of any BMS comments; and

(d) discussion of any other topics or issues relating to the Combined Therapy Clinical Trial requested by the Recipient or BMS.

2.4 Conduct. Each Party shall use Commercially Reasonable Efforts to (a) perform and fulfill its respective activities under the Combined Therapy Clinical Trial and this Agreement on a timely basis and in an effective manner consistent with prevailing standards, (b) supply the quantities of its Study Drug in accordance with Article 4 as needed to conduct the Combined Therapy Clinical Trial on a timely basis, and, in the case of the Recipient, package and deliver same to study sites on a timely basis, and (c) in the case of the Recipient, conduct and complete the Combined Therapy Clinical Trial on a timely basis in accordance with the Protocol and Third Party agreements relating thereto, and provide sufficient resources, funding and personnel to conduct and perform the Combined Therapy Clinical Trial on a timely basis in accordance with the Protocol for same and the terms of this Agreement. Each Party shall perform its duties for the Combined Therapy Clinical Trial in accordance with Applicable Law, including GCP, GLP and GMP as applicable.

2.5 [**].

ARTICLE 3

LICENSE GRANTS

3.1 Grants by BMS.

(a) BMS hereby grants, and shall cause its Affiliates to grant, to Recipient and Recipient's Affiliates a non-exclusive, worldwide (other than within the [**] or the [**] Territory), non-transferable, royalty-free license (with the right to sublicense solely pursuant to the terms of and subject to the limitations of Section 3.4) under the BMS Independent Patent Rights, BMS Technology and BMS Regulatory Documentation to use the BMS Study Drug in research and development, solely to the extent necessary to conduct the Combined Therapy Clinical Trial in the Territory in the Field subject to and in accordance with the terms and conditions of this Agreement and the Protocol.

(b) Subject to Section 3.3 below, BMS hereby grants, and shall cause its Affiliates to grant, to Recipient and Recipient's Affiliates a non-exclusive, worldwide (other than within the [**] or the [**] Territory), non-transferable (subject to Section 13.10), irrevocable, royalty-free license (with the right to sublicense solely pursuant to the terms of and subject to the limitations of Section 3.3) under the BMS Independent Patent Rights, BMS Technology and BMS Regulatory Documentation to seek Regulatory Approval of the Recipient Study Drug for use in a Combined Therapy in the Field, and, upon any such Regulatory Approval, to market and promote the Recipient Study Drug solely for use in a Combined Therapy in the Field in any manner that is consistent with the Regulatory Approval for the Recipient Study Drug. The right granted under this Section 3.1(b) includes a Right of Cross-Reference to the relevant BMS Regulatory Documentation solely to the extent necessary and solely for the purpose of obtaining Regulatory Approval outside the [**] and the [**] Territory in the Field for the Recipient Study Drug for use in a Combined Therapy based upon the Combined Therapy Clinical Trial (which right shall survive any expiration or termination of this Agreement). In such case, BMS shall reasonably cooperate with Recipient and make written authorizations and other filings with the applicable Regulatory Authority reasonably required to effect such Right of Cross-Reference. For avoidance of doubt, no rights are granted under this Section 3.1(b) for the [**] or the [**] Territory and no rights are granted except for use in a Combined Therapy (i.e., use of the Recipient Study Drug in combination with the BMS Study Drug) in the Field, with no rights being granted for the use of any other compound or therapeutic agent other than the Recipient Study Drug in combination with the BMS Study Drug.

(c) BMS hereby grants, and shall cause its Affiliates to grant, to Recipient and Recipient's Affiliates a non-exclusive, worldwide (other than with respect to the [**] and the [**] Territory) non-transferable (subject to Section 13.10), irrevocable, royalty-free license (with the right to sublicense solely pursuant to the terms of and subject to the limitations of Section 3.3) in the Field under the BMS Study Inventions and BMS Study Patent Rights for all purposes in the Field except to research, develop, make,

have made, use, sell offer for sale, export or import the BMS Study Drug or any biosimilar version of the BMS Study Drug.

3.2 Grants by Recipient.

(a) Recipient hereby grants, and shall cause its Affiliates to grant, to BMS and BMS' Affiliates a non-exclusive, worldwide (other than within the [**] or the [**] Territory), non- transferable, royalty-free license (with the right to sublicense solely pursuant to the terms of and subject to the limitations of Section 3.3) under the Recipient Independent Patent Rights, Recipient Technology and Recipient Regulatory Documentation to use the Recipient Study Drug in research and development, solely to the extent necessary to conduct the Combined Therapy Clinical Trial in the Territory in the Field subject to and in accordance with the terms and conditions of this Agreement.

(b) Subject to Section 3.3 below, Recipient hereby grants, and shall cause its Affiliates to grant, to BMS and BMS' Affiliates a non-exclusive, worldwide (other than within the [**] or the [**] Territory) non-transferrable (subject to Section 13.10), irrevocable, royalty-free license in the Field (with the right to sublicense solely pursuant to the terms of and subject to the limitations of Section 3.3) under the Recipient Independent Patent Rights, Recipient Technology and Recipient Regulatory Documentation to seek Regulatory Approval of the BMS Study Drug for use in a Combined Therapy in the Field, and, upon any such Regulatory Approval, to market and promote the BMS Study Drug solely for use in a Combined Therapy in the Field in any manner that is consistent with the Regulatory Approval for the BMS Study Drug. The right granted under this Section 3.2(b) includes a Right of Cross-Reference to the relevant Recipient Regulatory Documentation solely to the extent necessary and solely for the purpose of obtaining Regulatory Approval outside the [**] or the [**] Territory in the Field in the Territory for the BMS Study Drug for use in a Combined Therapy based upon the Combined Therapy Clinical Trial (which right shall survive any expiration or termination of this Agreement). In such case, Recipient shall reasonably cooperate with BMS and make written authorizations and other filings with the applicable Regulatory Authority reasonably required to effect such Right of Cross-Reference. For avoidance of doubt, no rights are granted under this Section 3.2(b) for the [**] or the [**] Territory or outside of the Field and no rights are granted except for use in a Combined Therapy (i.e., use of the BMS Study Drug in combination with the Recipient Study Drug) in the Field, with no rights being granted for the use of any other compound or therapeutic agent other than the BMS Study Drug in combination with the Recipient Study Drug.

(c) Recipient hereby grants, and shall cause its Affiliates to grant, to BMS and BMS' Affiliates a non-exclusive, worldwide (other than within the [**] or the [**] Territory), non- transferable (subject to Section 13.10), irrevocable, royalty-free license in the Field (with the right to sublicense solely pursuant to the terms of and subject to the limitations of Section 3.3) under the Recipient Study Inventions and Recipient Study Patent Rights for all purposes in the Field except to research, develop, make, have made, use, sell offer for sale, export or import the Recipient Study Drug or any biosimilar version of the Recipient Study Drug.

3.3 Sublicensing.

(a) Each Party shall have the right to grant sublicenses under the licenses granted to it under Section 3.1(a) and 3.2(a) to Affiliates and, if required for a Third Party to perform its duties (to the extent permitted under the terms and conditions of this Agreement), to Third Parties, solely as necessary to assist a Party in carrying out its responsibilities with respect to the Combined Therapy Clinical Trial. Each Party shall have the right to grant sublicenses under the licenses granted to it under Section 3.1(b) and (c) and Section 3.2(b) and (c) to Affiliates and, with respect to Recipient, to [**] solely within the [**] Territory. For the avoidance of doubt neither Party nor any of their Affiliates or sublicensees will have the right to grant any sublicenses within the Ono Territory under the licenses granted to it under Section 3.1 or Section 3.2.

(b) With regard to any such sublicenses permitted and made under this Agreement, (i) such sublicensees, except Affiliates (so long as they remain Affiliates of a Party), shall be subject to written

agreements that bind such sublicensees to obligations that are consistent with a Party's obligations under this Agreement including, but not limited to, confidentiality and non-use provisions similar to those set forth in Article 8 and Article 9, and provisions regarding intellectual property that ensure that the Parties will have the rights provided under this Agreement to any intellectual property created by such sublicensee, (ii) each Party shall provide written notice to the other of any such sublicense (and obtain written approval for sublicenses to Third Parties not contemplated by the Protocol for the Combined Therapy Clinical Trial) and (iii) the licensing Party shall remain liable for all actions of its sublicensees. For clarity, any agreements with CROs and other contractor/vendors, and Site Agreements and CRO Agreements shall be subject to the provisions of Section 2.1 (and other terms and conditions of the Agreement).

3.4 Rights for Combined Therapy Patents. The rights of the Parties with respect to the Combined Therapy Inventions and Combined Therapy Patents are set forth in Article 6.

3.5 Use of Study Data and Samples. The rights of the Parties with respect to the use and disclosure of the Study Data and the use of Samples are set forth in Article 8.

3.6 No Implied Licenses. Except as specifically set forth in this Agreement, neither Party shall acquire any license or other intellectual property interest, by implication or otherwise, in any intellectual property of the other Party, including Confidential Information disclosed to it under this Agreement or under any Patent Rights Controlled by the other Party or its Affiliates. Except for the licenses granted under Section 3.1 and 3.2, nothing in the Agreement is intended or shall be construed as granting either Party any right or license, expressly or impliedly, to make, have made, use, sell, offer for sale or import the other Party's Study Drug.

ARTICLE 4

MANUFACTURE AND SUPPLY

4.1 Recipient Study Drug Manufacture and Supply.

(a) The Recipient shall be responsible, at its sole costs and expense, for manufacturing, packaging and labeling (or having manufactured, packaged or labeled) GMP-grade quantities of the Recipient Study Drug, as well as obtaining any other drug (other than the BMS Study Drug provided by BMS pursuant to Section 4.2) required for the conduct of the Combined Therapy Clinical Trial, and shall package and label if and as required by the Protocol and/or applicable Regulatory Authorities all drugs (including the BMS Study Drug) used in the Combined Therapy Clinical Trial, on a timely basis and in accordance with applicable specifications as required for the conduct of the Combined Therapy Clinical Trial. The Recipient Study Drug shall be manufactured in accordance with Applicable Law (including GMP) and shall be of similar quality to the Recipient Study Drug used by the Recipient for its other clinical trials of the Recipient Study Drug.

(b) The Recipient shall provide BMS with prompt notice of any Manufacturing and supply issues with respect to the Recipient Study Drug or BMS Study Drug that may adversely impact the conduct or timelines of the Combined Therapy Clinical Trial.

4.2 BMS Study Drug.

(a) Manufacture and Supply. BMS shall Manufacture or have Manufactured the BMS Study Drug in reasonable quantities needed, and at the points in time as agreed to by the Parties, for the Combined Therapy Clinical Trial, and shall supply such BMS Study Drug as commercially labeled or unlabeled vials to the Recipient or its designee for use solely in the Combined Therapy Clinical Trial. The Recipient will at its sole expense, package and label the BMS Study Drug for use in the Combined Therapy Clinical Trial to the extent necessary. The cost of Manufacture and supply (including shipping, taxes and duty, if applicable) of the BMS Study Drug for the Combined Therapy Clinical Trial shall be borne solely by BMS, and BMS shall bear the risk of loss for such quantities of BMS Study Drug until delivery of such quantities of BMS Study Drug to the Recipient or its designee. BMS shall also be responsible for the

payment of any Third Party License Payments that may be due based on the manufacture, supply and use of the BMS Study Drug used in the Combined Therapy Clinical Trial. The BMS Study Drug shall be manufactured in accordance with Applicable Law (including GMP) and shall be of similar quality to the BMS Study Drug used by BMS for its other clinical trials of the BMS Study Drug. BMS shall deliver certificates of analysis, and any other documents specified in the Supply and Quality Documentation, including such documentation as is necessary to allow the Recipient to compare the BMS Study Drug certificate of analysis to the BMS Study Drug specifications. Pursuant to the Supply and Quality Documentation, BMS shall be responsible for the regulatory compliance of the quality of the BMS Study Drug at the time the BMS Study Drug is delivered to the Recipient with the regulatory filings in the countries in the Territory where the Combined Therapy Clinical Trial will be performed. Subject to Section 4.4, the Parties shall cooperate in accordance with Applicable Law to minimize indirect taxes (such as value added tax, sales tax, consumption tax and other similar taxes) relating to the BMS Study Drug in connection with this Agreement.

(b) Use of BMS Study Drug Supplied by BMS to the Recipient. The Recipient shall use the quantities of BMS Study Drug supplied to it under this Agreement solely as necessary for, and in accordance with, this Agreement and the Protocol, and for no other purpose, including as a reagent or tool to facilitate its internal research efforts, for any commercial purpose, or for other clinical or non-clinical research unrelated to the Combined Therapy Clinical Trial. Except as may be required or expressly permitted by the Protocol or the Supply and Quality Documentation, the Recipient shall not perform, and shall not allow any Third Party to perform, any analytical testing of the quantities of BMS Study Drug supplied to it under this Agreement. If Study Drug supplied by BMS is lost, damaged, destroyed or becomes unable to comply with applicable specifications while under the control of the Recipient or any of its (sub)contractors, including common carriers and clinical study sites contracted by the Recipient, BMS shall not be obligated to replace same, and if BMS does elect to do so, BMS may elect to charge the Recipient a reasonable replacement cost to replace same.

4.3 Supply and Quality Documentation. BMS shall supply the BMS Study Drug to the Recipient in accordance with such supply and quality addenda or agreement(s) as the Parties may agree (the "Supply and Quality Documentation"). The Parties shall finalize and execute the Supply and Quality Documentation after the Effective Date, but in no event later than the date on which the first shipment of the BMS Study Drug is supplied for use in the Combined Therapy Clinical Trial. The Supply and Quality Documentation shall outline the additional roles and responsibilities relative to the quality of BMS Study Drug in support of the Combined Therapy Clinical Trial. It shall include the responsibility for quality elements as well as exchanged GMP documents and certifications required to release the BMS Study Drug for the Combined Therapy Clinical Trial. In addition, the Supply and Quality Documentation shall detail the documentation required for each shipment of BMS Study Drug supplied to the Recipient or its designee for use in the Combined Therapy Clinical Trial.

4.4 Supply Forecast. Estimated supply and delivery details will be outlined in the Supplyand Quality Documentation and will be updated by the Parties by mutual agreement (which agreement can be effected by the Parties' Designated Supply contacts and without need for an amendment to this Agreement) based on the actual enrollment. The Recipient will promptly inform BMS of any change in its requirements, and BMS will endeavor to accommodate any change in the supply quantities requested by the Recipient so long as it does not unduly disrupt BMS's ongoing business activities.

4.5 Shortages. In the event of a supply interruption or shortage of BMS Study Drug as determined by BMS pursuant to its internal processes and policies (a "Shortage"), such that BMS reasonably believes that it will not be able to fulfill its supply obligations under this Agreement, BMS will provide prompt written notice thereof to the Recipient (including the quantity of BMS Study Drug that BMS reasonably estimates it will be able to supply) and, upon request, the Parties will promptly discuss such situation (including how the quantities of BMS Study Drug that BMS is able to supply under this Agreement will be allocated within the Combined Therapy Clinical Trial). Notwithstanding anything to the contrary contained herein, in the event of a Shortage of the BMS Study Drug, BMS will have sole discretion, subject to Applicable Law, to

determine the quantity of BMS Study Drug it will be able to supply as a result of such Shortage; provided, however, that BMS shall consider in good faith the needs of patients who are actively being treated with BMS Study Drug, including Combined Therapy Clinical Trial patients, in making such determination. BMS will not be deemed to be in breach of this Agreement for failure to supply any other quantities of BMS Study Drug hereunder as a result of a Shortage. Any such allocation of the BMS Study Drug in accordance with this Section 4.5 will the Recipient's exclusive remedy with respect to a Shortage.

4.6 Customs Valuation. The Recipient will provide BMS in writing with a list of each country in which it proposes to conduct the Combined Therapy Clinical Trial prior to execution of any site agreement or CRO agreement for that country. During the conduct of the Combined Therapy Clinical Trial, the Recipient will send in writing any changes to the list of participating countries to BMS one month prior to the end of each Quarter. If no changes are sent to BMS by the Recipient for a particular Quarter, the prior Quarter's participating country list will be used as the basis for customs valuation for that Quarter. BMS will provide the Recipient with country-specific customs valuations initially for the BMS Study Drug prior to initiation of the Combined Therapy Clinical Trial. The expiration date(s) of the customs value(s) will be monitored by the Recipient and the Recipient will send a request in writing to BMS to provide updated customs value(s) and expiration date(s) at least 30 days in advance of any customs value expirations The Recipient will use the BMS provided values for the import/export process to the listed participating countries and not make any change to such valuations without BMS's prior written consent.

4.7 Designated Supply Contact. Each Party will designate an individual (the "Designated Supply Contact") that a Party may contact to assist with coordinating supplies and facilitating the resolution of any issues or concerns arising in connection with the supply of the BMS Study Drug for use in the Combined Therapy Clinical Trial.

ARTICLE 5

RESPONSIBILITIES

5.1 Specific Responsibilities of the Recipient. The Recipient shall, subject to the terms of the Protocol, applicable terms and conditions of this Agreement, and any other agreement between the Parties relating to the Combined Therapy Clinical Trial, manage and be responsible for the conduct of the Combined Therapy Clinical Trial, including timelines and contingency planning. In particular, and not in limitation of the foregoing, the Recipient shall perform (itself and/or through Third Parties, including clinical trial sites, CROs and investigators) and/or be responsible for the following (items (a) to (p) below), collectively the "Operational Matters") with respect to the Combined Therapy Clinical Trial:

(a) compiling, amending and filing all necessary Combined Therapy Clinical Trial Regulatory Documentation with Regulatory Authority(ies), maintaining and acting as the sponsor of record as provided in 21 CFR 312.50 (and applicable comparable ex-US laws) with responsibility, unless otherwise delegated in accordance with 21 CFR 312.52 (and applicable comparable ex-US laws), for the Combined Therapy Clinical Trial and making all required submissions to Regulatory Authorities related thereto on a timely basis;

(b) conducting clinical study start-up activities, communicating with and obtaining approval from IRBs for the Protocol and other relevant documents for the Combined Therapy Clinical Trial as applicable, as well as patient recruitment and retention activities;

(c) listing of the Combined Therapy Clinical Trial, if it is required to be listed on a public database on www.clinicaltrials.gov or other public registry in any country in which such Combined Therapy Clinical Trial is being conducted, all in accordance with Applicable Law and in accordance with its internal policies relating to clinical trial registration;

(d) providing BMS with reasonable advance notice of meetings or other non-written communications with a Regulatory Authority and the opportunity to participate in each such meeting or

other non-written communication, to the extent involving a safety, efficacy or toxicology issue relating to the Combined Therapy or the BMS Study Drug or any other matter that could have an adverse effect on the BMS Study Drug. In such case, the Recipient will provide BMS with the opportunity to review, provide comments to the Recipient within [**] on, and, if inconsistent with the Protocol, approve all submissions and written correspondence with a Regulatory Authority that relates to the BMS Study Drug;

(e) provide BMS (i) a written summary of meetings or other non-written communications with a Regulatory Authority within [**] of such meeting or communication, and (ii) copies of any official correspondence to or from a Regulatory Authority within [**] of receipt or provision, in each case of (i) or (ii) to the extent involving a safety, efficacy or toxicology issue relating to the Combined Therapy or the BMS Study Drug or any other matter that could have an adverse effect on the BMS Study Drug, and copies of all material Combined Therapy Clinical Trial Regulatory Documentation and correspondence that relates to same within [**] of submission to Regulatory Authorities;

(f) subject to the terms of this Agreement, the selection and payment of, negotiation of the terms of, contracting with, managing and overseeing compliance of its agreement by and the receipt of contract deliverables from, any CRO or vendor selected by the Recipient to assist in the performance of the Combined Therapy Clinical Trial. The Recipient shall determine and approve contract deliverables and manage contract performance, including executing site contracts, drafting and obtaining IRB approval for site informed consent forms (each an "ICF"), obtaining signed ICFs, monitoring plans, etc. The Recipient will be responsible for ensuring that all such contracts and ICFs: (i) do not conflict with the terms of this Agreement, (ii) allow the Recipient to provide BMS with access to and use of Study Data, Samples, and other information and documents as required pursuant to this Agreement (and in no event less than the same use rights granted to the Recipient), (iii) do not adversely affect the BMS Technology or BMS Independent Patent Rights (or the enforcement or defense thereof), the [**], the Combined Therapy, or the BMS Study Drug as monotherapy, (iv) do not impose a new obligation, whether direct, indirect, or contingent, upon BMS that is not set forth in this Agreement, (v) do not confer a benefit upon the Recipient that is not also conferred upon BMS, (vi) retain each of the Parties' respective intellectual property rights in the Recipient Study Drug, BMS Study Drug and Combined Therapy consistent with this Agreement, and (vii) comply with Applicable Law;

(g) providing BMS a copy of the protocol level ICF template for the Combined Therapy Clinical Trial and (if requested by BMS) with copies of each final site template of the Combined Therapy Clinical Trial's ICF. The Recipient shall ensure that each ICF does not impose any financial obligation, liability, damages or other cost upon BMS with respect to any injury (including death) suffered by a Combined Therapy Clinical Trial subject whether or not resulting from the administration of the BMS Study Drug or direct a study subject to BMS to seek reimbursement for any costs or seek compensation for any injury incurred in connection with the Combined Therapy Clinical Trial;

(h) providing BMS within [**] with minutes from any and all external drug safety monitoring boards for the Combined Therapy Clinical Trial after receipt by the Recipient, to the extent relating to the BMS Study Drug or the Combined Therapy;

(i) informing and updating BMS on a monthly basis (with significant issues to be communicated promptly after the Recipient becomes aware of same) regarding all Operational Matters, so that if BMS has any significant concerns or material disagreements regarding same, the matter can be discussed with the Recipient. Without limiting the foregoing, the Recipient shall inform BMS monthly as to the overall Combined Therapy Clinical Trial progress, information regarding the number and status of study sites, the number of screened subjects (actual to target), the number of any randomized subjects (actual to target), the number of dosed, ongoing, discontinued and completed subjects, any safety updates as contemplated by the Protocol, and/or routinely performed by the Recipient in its normal course of trial management and reporting, and any other Combined Therapy Clinical Trial-related matters requested by BMS to the extent involving a safety, efficacy or toxicology issue relating to the Combined Therapy or the BMS Study Drug or any other matter that could have an adverse effect on the BMS Study Drug;

(j) owning and being responsible for (or appointing a Third Party to be responsible for) the maintenance of the Global Safety Database and being responsible for safety reporting, collecting, evaluating and reporting Serious Adverse Events, other safety data and any further pharmacovigilance information from the Combined Therapy Clinical Trial;

(k) analyzing the Study Data in a timely fashion and providing BMS with access to the Study Data as follows:

(i) top line results and a copy of all Clinical Study Reports (CSRs), in each case, as and when received by the Recipient's clinical management;

(ii) if requested by BMS, sharing with BMS for review and comment drafts of interim and/or final clinical trial report (and/or statistical analysis in accordance with the Protocol) from the Combined Therapy Clinical Trial;

(iii) if requested by BMS, within [**] Business Days after database lock, access to those safety databases that will be used for any interim review by an external consultant (or drug safety monitoring board, if required);

(iv) if requested by BMS, within [**] Business Days after database lock, access to case report forms or patient profiles for all patients in the Combined Therapy Clinical Trial;

(v) if requested by BMS, within [**] Business Days of the creation of an electronic clean database for the Combined Therapy Clinical Trial, an electronic copy of both the raw and clean databases (the form and format of the clean and raw databases to be reasonably acceptable to both Parties);

(vi) if requested by BMS, subject to any third party requirements, providing BMS with any programs or SAS codes to be used for any statistical analysis plan for the Combined Therapy Clinical Trial; and

(vii) (A) safety analyses, (B) new and/or changing Safety Signals and Safety Issues, (C) new and/or changing toxicology and efficacy signals, and (D) any statistical analysis, immunogenicity analysis, or bioanalysis, in each case relating to the BMS Study Drug, the Recipient Study Drug and/or the Combined Therapy, as and when the same are received by the Recipient;

(l) obtaining supplies of any co-medications, to the extent any such co-medications are required for use in the Combined Therapy Clinical Trial, and providing to BMS any information related to the Combined Therapy Clinical Trial that is provided to the manufacturer of any co-medication within [**] after the provision of the information to the manufacturer;

(m) if requested by BMS, information regarding the pharmacokinetics, efficacy and safety of the Recipient Study Drug alone or in combination with the BMS Study Drug;

(n) performing either directly or through third parties collection of Samples required by the Protocol;

(o) handling and addressing inquiries from the Combined Therapy Clinical Trial subjects and investigators, and;

(p) such other responsibilities as may be agreed to by the Parties

5.2 BMS Operational Responsibilities. BMS shall be responsible for the following activities:

(a) Manufacturing and supplying GMP-grade quantities of the BMS Study Drug, as further described in Article 4 above, and, where and to the extent provided in the Supply and Quality

Documentation, providing necessary GMP information and documentation that enables the Recipient Qualified Person (as such term will be defined in the Supply and Quality Documentation) to release BMS Study Drug for the Combined Therapy Clinical Trial;

(b) where and to the extent provided in the Supply and Quality Documentation, providing for the release by a Qualified Person or providing the necessary documentation in support of such quality release, of the BMS Study Drug if such release is required for the Combined Therapy Clinical Trial;

(c) to the extent necessary for the conduct of the Combined Therapy Clinical Trial, providing a Right of Cross-Reference to the relevant Regulatory Documentation for the BMS Study Drug as set forth in Section 2.1(b) and/or (e), if applicable, to the BMS investigator's brochure for the BMS Study Drug (and updates thereto) as provided in Section 2.1(d); and

(d) such other responsibilities as may be agreed to by the Parties.

5.3 Other Clinical Trials. Nothing in this Agreement shall preclude either Party from conducting any other clinical trials as it may determine in its discretion, so long as it does not use or rely on the Confidential Information that is solely owned by the other Party in doing so.

5.4 Potential Subsequent Studies. After completion of the Combined Therapy Clinical Trial, the Parties agree to discuss in good faith additional Combined Therapy Clinical Trials of the BMS Study Drug with the Recipient Study Drug. If the Parties jointly agree to conduct any such further clinical trials, such further clinical trials will, unless otherwise mutually agreed in writing, be conducted in accordance with a separate agreement.

ARTICLE 6

INTELLECTUAL PROPERTY

6.1 Inventions and related Patent Rights. All rights to Inventions shall be allocated as follows:

(a) Recipient Ownership. Subject to the terms of this Agreement, all Recipient Study Inventions and Recipient Study Patent Rights shall be owned solely by the Recipient, and the Recipient will have the full right to exploit such Recipient Study Inventions and Recipient Study Patent Rights without the consent of, or any obligation to account to, BMS. BMS shall assign and hereby assigns (and shall cause its Affiliates and contractors to assign) its right, title and interest in any Recipient Study Inventions and Recipient Study Patent Rights to the Recipient. BMS shall execute such further documents and provide other assistance as may be reasonably requested by the Recipient to perfect the Recipient's rights in such Recipient Study Inventions and Recipient Study Patent Rights, all at the Recipient's expense. The Recipient shall have the sole right but not the obligation to prepare, file, prosecute (including any proceedings relating to reissues, reexaminations, protests, interferences, oppositions, post-grant reviews or similar proceedings and requests for patent extensions) and maintain any Recipient Study Patent Rights at its own expense.

(b) BMS Ownership. Subject to the terms of this Agreement, all BMS Study Inventions and BMS Study Patent Rights shall be owned solely by BMS, and BMS will have the full right to exploit such BMS Study Inventions and BMS Study Patent Rights without the consent of, or any obligation to account to, the Recipient. The Recipient shall assign and hereby assigns (and shall cause its Affiliates and contractors to assign) all its right, title and interest in any BMS Study Inventions and BMS Study Patent Rights to BMS. The Recipient shall execute such further documents and provide other assistance as may be reasonably requested by BMS to perfect BMS's rights in such BMS Study Inventions and BMS Study Patent Rights, all at BMS's expense. BMS shall have the sole right but not the obligation to prepare, file, prosecute (including any proceedings relating to reissues, reexaminations, protests, interferences, oppositions, post-grant reviews or similar proceedings and requests for patent extensions) and maintain any BMS Study Patent Rights at its own expense.

(c) Combined Therapy Inventions. All Combined Therapy Inventions and Combined Therapy Patent Rights shall be jointly owned by the Parties, and either Party shall have the right to freely exploit the Combined Therapy Inventions and Combined Therapy Patent Rights, both within and outside the scope of this Agreement, without accounting or any other obligation to the other Party (except as expressly set forth in this Section 6.1(c) and Section 6.3(d) with regard to the filing, prosecution, maintenance and enforcement of Combined Therapy Patent Rights) and each Party may use, exploit and grant licenses (with right to sublicense) to Third Parties under its interest in such Combined Therapy Inventions and Combined Therapy Patent Rights. The Recipient, using outside counsel acceptable to both Parties, shall be responsible, at its sole discretion, for preparing and prosecuting Patent applications and maintaining Patents within the Combined Therapy Patent Rights. The Recipient shall keep BMS advised as to material developments and steps to be taken with respect to prosecuting any such Patent Rights and shall furnish BMS with copies of applications for such Patent Rights, amendments thereto and other related correspondence to and from patent offices, and permit BMS a reasonable opportunity to review and offer comments prior to submitting such applications and correspondence to the applicable governmental authority (and will take BMS's comments into account in preparing same). BMS shall reasonably assist and cooperate in obtaining, prosecuting and maintaining the Combined Therapy Patent Rights. The Recipient shall be reimbursed for any costs and expenses incurred in prosecuting Combined Therapy Patent Rights and the subsequent maintenance of Combined Therapy Patent Rights by BMS such that BMS shall be responsible for [**]. From time-to-time, the Recipient shall invoice BMS such amounts and BMS shall pay the Recipient such invoiced amounts within [**] after receipt of an invoice therefor. The Parties shall discuss in good faith the countries in which the Combined Therapy Patent Rights will be filed. In case one of the two Parties decides not to file or maintain a Combined Therapy Patent Right in a given country (and also elects not to reimburse the other Party for [**] of prosecution and maintenance of such Combined Therapy Patent Right in such country), the other Party shall have the right to file, prosecute and maintain such Combined Therapy Patent Right in such country in its own name and at its own expense. In this case, the Party who decides not to file or maintain (and also decides not to reimburse the other Party for its share of the costs of) a Combined Therapy Patent Right for a given country shall promptly assign its rights to the Combined Therapy Patent Right in said country to the Party (the "Filing Party") who wishes to file or maintain said Combined Therapy Patent Right in such country and the Filing Party shall grant, and hereby grants, to the other Party an irrevocable, perpetual, fully-paid, non-exclusive license, with the right to grant and authorize sublicenses, under such Combined Therapy Patent Rights to make, have made, use, sell, offer for sale, import and other exploit products and services in such country. The Party who does not wish to file or maintain a Combined Therapy Patent Right in any country shall assist in the timely provision of all documents required under national provisions to register said assignment of rights with the corresponding national authorities at the sole expenses of the Party who wishes to file or maintain such Combined Therapy Patent Right in that given country. If the Parties cannot agree with respect to the decision to file or maintain a Combined Therapy Patent Right within [**] subsequent to the initiation of the Parties' good faith efforts to resolve any disagreement, then either Party shall have the right to file or maintain any Combined Therapy Patent Right in the names of both Parties, provided that: (i) any such Combined Therapy Patent Right shall be jointly owned by the Parties and subject to the freedom to use and operate under such Combined Therapy Patent Right as set forth in the first sentence of this Section 6.1(c); (ii) such prosecuting Party obtains the prior consent of the non-prosecuting Party, which consent shall not be unreasonably withheld or delayed, and (iii) the non-prosecuting party reimburses the prosecuting party for its [**] of the patent costs. Notwithstanding the foregoing provisions in this Section 6.1(c), neither Party shall knowingly take any position in a submission to a patent office concerning a Combined Therapy Invention that interprets the scope of a Patent Right of the other Party without the prior written consent of such other Party.

(d) Separation of Patent Rights. In order to more efficiently enable the prosecution and maintenance of the BMS Study Patent Rights, the Recipient Study Patent Rights and Combined Therapy Patent Rights relating to Inventions as described above, the Parties will use good faith efforts to separate BMS Study Patent Rights, the Recipient Study Patent Rights, Combined Therapy Patent Rights, BMS Independent Patent Rights and the Recipient Independent Patent Rights into separate patent filings to the extent possible and without adversely impacting such prosecution and maintenance or the scope of the protected subject matter.

6.2 Disclosure and Assignment of Inventions. Each Party shall disclose promptly to the other Party in writing and on a confidential basis all Inventions, prior to any public disclosure thereof or filing of Patent Rights therefor and allowing sufficient time for comment by the other Party. In addition, each Party shall, and does hereby, assign, and shall cause its Affiliates and contractors to so assign, to the other Party, without additional compensation, such right, title and interest in and to any Inventions as well as any Patent Rights and other intellectual property rights with respect thereto, as is necessary to fully effect, as applicable, the sole ownership provided for in Sections 6.1(a) and 6.1(b) and the joint ownership provided for in Section 6.1(c).

6.3 Infringement of Patent Rights by Third Parties.

(a) Notice. Each Party shall promptly notify the other Party in writing of any Infringement of Combined Therapy Patent Rights, of which its in-house patent counsel becomes aware.

(b) Infringement of Recipient Study Patent Rights. For all Infringements of Recipient Study Patent Rights anywhere in the world, the Recipient shall have the exclusive right to prosecute such Infringements as it may determine in its sole and absolute discretion, and the Recipient shall bear all related expenses and retain all related recoveries. BMS shall reasonably cooperate with the Recipient or its designee (to the extent BMS has relevant information arising out of this Agreement), at the Recipient's request and expense, in any such action.

(c) Infringement of BMS Study Patent Rights. For all Infringements of BMS Study Patent Rights anywhere in the world, BMS shall have the exclusive right to prosecute such Infringements as it may determine in its sole and absolute discretion, and BMS shall bear all related expenses and retain all related recoveries. The Recipient shall reasonably cooperate with BMS or its designee (to the extent that the Recipient has relevant information arising out of this Agreement), at BMS's request and expense, in any such action.

(d) Infringement of Combined Therapy Patent Rights.

(i) With respect to Infringements of Combined Therapy Patent Rights, the Parties shall mutually agree as to whether to bring an enforcement action to seek the removal or prevention of such Infringements and damages therefor and, if so, which Party shall bring such action, with any costs and expenses relating thereto to be allocated in accordance with Section 6.3(d)(ii).

(ii) Regardless of which Party brings an enforcement action pursuant to Section 6.3(d)(i) or whether the Parties reach agreement to initiate such an enforcement action, the other Party hereby agrees to cooperate reasonably in any such action, including, if required, by bringing a legal action, furnishing a power of attorney or joining as a plaintiff to such a legal action. If the Parties mutually agree to bring an enforcement action, BMS shall be responsible for [**] percent ([**]%), and the Recipient shall be responsible for [**] percent ([**]%), of the reasonable and verifiable costs and expenses incurred in connection with any such action. If either Party recovers monetary damages from any Third Party in an action agreed to by the Parties, such recovery shall be allocated first to the reimbursement of any actual, unreimbursed costs and expenses incurred by the Parties in such litigation (including, for this purpose, a reasonable allocation of expenses of internal counsel) pro rata in accordance with the aggregate amounts spent by both Parties, and any remaining amounts shall be [**] percent ([**]%) to the Recipient and [**] percent ([**]%) to BMS, unless the Parties agree in writing to a different allocation. If the Parties do not agree to initiating such an enforcement action, (A) the Party initiating such enforcement action shall be responsible for the costs and expenses incurred in connection with such action and shall reimburse the other Party for the costs the other Party incurs for the assistance and cooperation requested by such Party and (B) the Party initiating such enforcement action shall retain all recoveries from such enforcement action. Neither Party shall enter into any settlement without the prior written consent of the other Party in connection with any proceeding under this Section 6.3(d).

6.4 Infringement of Third Party Rights.

(a) Notice. If the activities relating to the Combined Therapy Clinical Trial become the subject of a claim of infringement of a patent, copyright or other proprietary right by a Third Party anywhere in the world, the Party first having notice of the claim shall promptly notify the other Party and, without regard to which Party is charged with said infringement and the venue of such claim, the Parties shall promptly confer to discuss the claim.

(b) Defense. If both Parties are charged with infringement pursuant to a claim described in Section 6.4(a), each Party shall have the right to defend itself against such claim and the Parties shall discuss in good faith defending such claim jointly. If only one Party is charged with infringement, such Party will have the first right but not the obligation to defend such claim. If the charged Party does not commence actions to defend such claim within [**] after request by the other Party to do so, then the other Party shall have the right, but not the obligation, to defend any such claim to the extent such claim pertains to the other Party's Study Drug. In any event, the non-defending Party shall reasonably cooperate with the Party conducting the defense of the claim and shall have the right to participate with separate counsel at its own expense, and the defending Party shall consider comments and suggestions on strategy for defending the action by the non-defending Party in good faith. The Party defending the claim shall bear the cost and expenses of the defense of any such Third Party infringement claim and shall have sole rights to any recovery. If the Parties jointly defend the claim, the Recipient shall bear [**], and BMS shall bear [**] of any costs and expenses of the defense of any such Third Party infringement claim; provided, however, that, notwithstanding the foregoing, if the claim relates solely to one Party's Study Drug, such Party will bear [**] of the costs and expenses of the defense of such claim and shall have the sole right, but not the obligation, to defend, settle and otherwise handle the disposition of such claim. Neither Party shall enter into any settlement concerning activities under this Agreement or the Combined Therapy that affects the other Party's rights under this Agreement or imposes any obligations on the other Party, including any admissions of wrongdoing on behalf of the other Party, without such other Party's prior written consent, not to be unreasonably withheld or delayed, except that a Party may settle any claim that solely relates to its Study Drug without the consent of the other Party as long as such other Party's rights under this Agreement are not adversely impacted (in which case, it will obtain such other Party's prior written consent, not to be unreasonably withheld or delayed).

6.5 Combined Therapy Clinical Trial Regulatory Documentation. Subject to the license and other rights granted by each Party to the other Party pursuant to this Agreement, the Recipient shall solely own all right, title and interest in and to the Combined Therapy Clinical Trial Regulatory Documentation; provided, however, that BMS shall retain sole and exclusive ownership of any BMS Regulatory Documentation that is submitted with or referenced in the Combined Therapy Clinical Trial Regulatory Documentation and that the Recipient shall retain sole and exclusive ownership of any Recipient Regulatory Documentation that is submitted with or referenced in the Combined Therapy Clinical Trial Regulatory Documentation. This Section 6.5 is without limitation of any other disclosure obligations under this Agreement.

6.6 No Other Use. Except as expressly provided in Section 6.1, the Recipient agrees not to apply for any Patent Rights based on or containing BMS Confidential Information, and to give no assistance to any Third Party for such application without BMS's prior written authorization, and BMS agrees not to apply for any Patent Rights based on or containing the Recipient's Confidential Information, and to give no assistance to any Third Party for such application without the Recipient's prior written authorization.

6.7 Joint Research Agreement. The Parties acknowledge and agree that this Agreement is a "joint research agreement" as defined in 35 USC § 100 (h).

ARTICLE 7

COSTS AND EXPENSES

7.1 Manufacturing and IP Costs. Expenses incurred as described in Article 4 (regarding Manufacturing and Supply) and Article 6 (regarding Intellectual Property) shall be borne or shared by the Parties as provided in such Articles.

7.2 TP Study Costs. For all expenses (other than those set forth in Section 7.1) that are directly attributable or reasonably allocable to the conduct of the Combined Therapy Clinical Trial: (a) [**] out-of-pocket costs reasonably incurred by [**] to Third Parties (including to CROs, laboratories and clinical sites/IRBs) in connection with the performance of the Combined Therapy Clinical Trial ("TP Study Costs"), and (b) [**] its own internal costs (including costs of individual independent contractors) incurred [**]. It is not expected that [**]; however, in the event [**] in connection with the conduct of the Combined Therapy Clinical Trial, the [**] for same on a quarterly basis within [**] following submission of an invoice therefor and appropriate supporting documentation.

7.3 Third Party License Payments. If the conduct of the Combined Therapy Clinical Trial requires a Third Party License Payment, then the Party required to make such payment shall be responsible for same.

ARTICLE 8

RECORDS AND STUDY DATA

8.1 Records. Each Party shall maintain complete and accurate records of all work conducted with respect to the Combined Therapy Clinical Trial and of all results, information, data, data analyses, reports, records, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences and developments made by or provided to either Party, or by the Parties together, in the course of such Party(ies)' efforts with respect to the Combined Therapy Clinical Trial, (such results, information, data, data analyses, reports, CRFs, adverse event reports, trial records, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, developments, and the Protocol referred to as the "Study Data"). Such records shall fully and properly reflect all work done and results achieved in the performance of the Combined Therapy Clinical Trial in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes.

8.2 Ownership of Study Data. BMS shall own the Study Data to the extent that it relates solely to the BMS Study Drug ("BMS Study Data"), and Recipient shall own the Study Data to the extent that it relates solely to the Recipient Study Drug ("Recipient Study Data").

8.3 Subject to the restrictions on use and disclosure as set forth in this Agreement, both Parties shall jointly own any Study Data that is not BMS Study Data or Recipient Study Data (such jointly owned Study Data being the "Combined Therapy Study Data"). Each Party shall, and does hereby, assign, and shall cause its Affiliates to so assign, to the other Party, [**], such right, title and interest in and to any Study Data as is necessary to fully effect the foregoing, and agrees to execute all instruments as may be reasonably necessary to effect same.

8.4 Use of a Party's Own Study Data. BMS may use, analyze and disclose to Third Parties the BMS Study Data for any purpose without obligation or accounting to Recipient. Recipient may use, analyze and disclose to Third Parties the Recipient Study Data for any purpose without obligation or accounting to BMS.

8.5 Use of Combined Therapy Study Data by BMS.

(a) Subject to the restrictions on disclosure of the Combined Therapy Study Data to Third Parties as set forth below in this Section 8.5, BMS shall have the right to use and analyze the Combined Therapy Study Data for any purpose.

(b) The Combined Therapy Study Data shall not be disclosed to Third Parties by BMS except as follows (and otherwise as expressly permitted under the Agreement).

(i) BMS may disclose the Combined Therapy Study Data to its contractors under confidentiality obligations similar to BMS' obligations under the Agreement, solely for purposes and to the extent required for such contractors to provide services for BMS for the development, regulatory approval and/or commercialization of the BMS Study Drug.

(ii) BMS may disclose the Combined Therapy Study Data (x) to Regulatory Authorities in connection with regulatory filings, (y) to investigators as necessary in connection with the Combined Therapy Clinical Trial and/or (y) as may be required by Applicable Law.

(iii) To the extent that the Combined Therapy Study Data includes safety information and BMS needs to disclose to Third Parties such safety information of the Combined Therapy in its studies of the BMS Study Drug with other cell based therapy in order to ensure patient safety, BMS may disclose such safety information. For clarity, BMS shall not disclose safety information related solely to the Recipient Study Drug.

(iv) BMS may use and disclose to a Third Party the Combined Therapy Study Data, under obligations of confidentiality consistent with this Agreement, to the extent such Third Party is developing or commercializing a biomarker or diagnostic test for use with its Study Drug and/or the Combined Therapy.

8.6 Use of Combined Therapy Study Data by Recipient.

(a) Subject to the restrictions on disclosure of the Combined Therapy Study Data to Third Parties as set forth below in this Section 8.6, Recipient shall have the right to use and analyze the Combined Therapy Study Data for any purpose.

(b) The Combined Therapy Study Data shall not be disclosed to Third Parties by Recipient except as follows (and otherwise as expressly permitted under the Agreement).

(i) Recipient may disclose the Combined Therapy Study Data to its contractors under confidentiality obligations similar to Recipient's obligations under the Agreement, solely for purposes and to the extent required for such contractors to provide services for Recipient for the development, regulatory approval and/or commercialization of the Recipient Study Drug.

(ii) Recipient may disclose the Combined Therapy Study Data (x) to Regulatory Authorities in connection with regulatory filings, (y) to investigators as necessary in connection with the Combined Therapy Clinical Trial and/or (y) as may be required by Applicable Law.

(iii) To the extent that the Combined Therapy Study Data includes safety information and Recipient needs to disclose to Third Parties such safety information of the Combined Therapy in its studies of the Recipient Study Drug with other compounds in order to ensure patient safety, Recipient may disclose such safety information solely for such purposes. For clarity, Recipient shall not disclose safety information related solely to the BMS Study Drug.

(iv) Recipient may use and disclose to a Third Party the Combined Therapy Study Data, under obligations of confidentiality consistent with this Agreement, to the extent such Third Party is developing or commercializing a biomarker or diagnostic test for use with its Study Drug and/or the Combined Therapy.

8.7 No Other Uses. All other uses of Study Data are limited solely to those permitted by this Agreement, and neither Party may use Study Data for any other purpose without the consent of the other Party during and after the Term of this Agreement.

8.8 Access to Study Data. In accordance with the terms and conditions of this Agreement, each Party shall have access to all Study Data (including the results of testing of Samples (including, but not limited to, de-identified patient records)) in a timely manner.

8.9 Samples.

(a) Samples collected in the course of activities conducted under this Agreement shall be jointly owned by the Parties (to the extent not owned by the patient and/or the clinical trial site). Any such Samples shall be collected in accordance with the applicable Protocol and ICFs. Neither Party shall be permitted to use the Samples for any purpose without the prior written consent of the other Party, which consent shall not be unreasonably withheld if such use is related to the Combined Therapy (with the terms of such use to be set forth in a written agreement between the Parties setting forth the Samples to be used, and any appropriate terms/restrictions on such use).

(b) Subject to Section 6.1 and 8.2, any data and Inventions (and Patent Rights claiming such Inventions) arising out of the permitted testing of the Samples shall be owned by the Party conducting such testing, provided that to the extent that any such data or Inventions (and Patent Rights claiming such Inventions) relates solely to the Combined Therapy (or biomarkers solely for use solely with the Combined Therapy), such data or Inventions (and Patent Rights claiming such Inventions) shall be considered Combined Therapy Study Data or Combined Therapy Inventions (and Combined Therapy Patents), as the case may be.

(c) The Parties will jointly decide on the selection of the repository for the Samples. If the Party holding the Samples determines that it no longer has a use for the Samples and the other Party determines that it does, then the Samples shall, subject to Applicable Law and the terms of the signed ICFs, be transferred to the other Party and may be used solely thereafter by the other Party. If neither Party has any further use for the Samples, then the remaining Samples will be destroyed pursuant to the respective Party's standard operating procedures for sample retention and destruction, subject to the terms of and permission(s) granted in the ICFs signed by the subjects contributing the Samples in the Combined Therapy Clinical Trial. [**].

8.10 NDAs and BLAs and their foreign equivalents. Notwithstanding either Party's ownership of (i) a Combined Therapy IND as set forth in Section 2.1(b) or (ii) Regulatory Documentation associated with a Combined Therapy IND, unless otherwise agreed by the Parties and reflected in writing, and pursuant to a regulatory submission strategy for the Combined Therapy based upon the Combined Therapy Study Data in the Field:

(a) The Parties (including their respective Affiliates and licensees) after top line results are provided per Section 5.1(k), will enter into good faith discussions to determine a regulatory submission strategy agreeable to both Parties for the applicable Combined Therapy indication based upon the Combined Therapy Study Data in the Field.

(b) With respect to filings within the United States or markets where a Party's Study Drug has achieved Regulatory Approval, if agreement on a regulatory submission strategy is not reached, then if such Party with Regulatory Approval desires to submit a filing to update its respective Study Drug's label for the Combined Therapy based upon the Combined Therapy Study Data, such Party (the "Filing Party") shall notify the other Party, and each Party and its Affiliates shall reasonably cooperate and take all steps reasonably necessary to enable such regulatory submission.

(c) In markets outside of the United States or where both Parties' Study Drugs have not achieved Regulatory Approval, the Parties (including their respective Affiliates and licensees) must agree on a regulatory submission strategy, and neither Party shall submit any regulatory filings for its respective Study Drug for the Combined Therapy based upon the Combined Therapy Study Data absent such agreement. Where the Parties mutually agree to file a regulatory submission, the Parties (including Affiliates and licensees) shall cooperate to take all steps reasonably necessary to enable such submission.

(d) The sponsor of record in the case of mutual agreement or the Filing Party in the case where agreement is not reached, shall prepare all Regulatory Documentation for any new or supplemental BLA or NDA and its foreign equivalent to be filed for a Combined Therapy arising from a Combined Therapy Clinical Trial. The sponsor of record in the case of mutual agreement or the Filing Party in the case where agreement is not reached, shall have primary responsibility, and shall have the first right but not the obligation, to file and maintain (directly or through its designee) any new or supplemental BLA or NDA and its foreign equivalent to be filed for a Combined Therapy arising from a Combined Therapy Clinical Trial for each Regulatory Authority (i.e., for each country or region); provided that the other Party (x) shall have the right to review and comment on all such Regulatory Documentation prior to such filing, as well as communications with Regulatory Authorities, (y) shall receive a complete, final copy of such Regulatory Documentation prior to such filing, and (z) shall have the right but not the obligation to file all such Regulatory Documentation on its own behalf concurrently or at any time thereafter (or at any time in the event that the Party having the first right to file elects not to file).

(e) For clarity, in the case of mutual agreement or the Filing Party in the case where agreement is not reached, each Party agrees to: (a) provide to the filing Party prompt, reasonable consultation and assistance with the preparation, filing and submission of Regulatory Documentation with the Regulatory Authorities, including providing access to all reasonably requested documentation under each Party's or its Affiliates' control that may be necessary or useful for the preparation of such Regulatory Documentation (including single-agent clinical data as reasonably required); and (b) complete all documents requested by the other Party reasonably required for such Regulatory Documentation, all in accordance with the timelines provided in this Agreement or otherwise agreed, and in any event such that final Regulatory Documentation is ready for filing with the applicable Regulatory Authority within a reasonable time period.

ARTICLE 9

CONFIDENTIALITY

9.1 Nondisclosure of Confidential Information.

Prior to the Effective Date, the Recipient and BMS entered into a certain Mutual Confidentiality Agreement dated October 2, 2018 (the "CDA"). As it relates to disclosures involving the BMS Study Drug, the Recipient Study Drug or the conduct of the Combined Therapy Clinical Trial only, the CDA is hereby terminated and replaced by the terms of this Agreement. Any Confidential Information relating thereto previously disclosed by the Parties pursuant to the CDA shall now be Confidential Information for purposes of this Agreement and the Parties shall treat it as such in accordance with the terms hereof. All written, visual, oral and electronic data, information, know-how or other proprietary information or materials, both technical and non-technical, disclosed by one Party to any other Party pursuant to this Agreement, and disclosed in the manner specified herein, that (a) if in tangible form, is labeled in writing as "proprietary" or "confidential" (or similar reference), or (b) if in oral or visual form, is identified as proprietary or confidential or for internal use only at the time of disclosure or within [**] thereafter shall be "Confidential Information" of the disclosing Party, and all Study Data and Inventions shall be the Confidential Information of the Party owning such Study Data or Invention (as provided in Section 8.2 with regard to Study Data and Section 6.1 with regard to Inventions). For purposes of this Agreement, regardless of which Party discloses such Confidential Information to the other, (i) all Recipient Study Inventions, Recipient Technology and Recipient Regulatory Documentation shall be Confidential Information of the Recipient and BMS shall be the receiving Party, (ii) all BMS Study Inventions, BMS Technology, and BMS Regulatory Documentation shall be Confidential Information of BMS and the Recipient shall be the receiving Party.

(a) The Parties agree that the terms of this Agreement shall be treated as Confidential Information of both Parties, and thus may be disclosed only as permitted by Section 9.3. Except as required by Applicable Law, each Party agrees not to issue any press release or public statement disclosing information relating to this Agreement or the transactions contemplated hereby or the terms hereof [**] of the other Party, except as permitted by Sections 9.3 and 9.5(b).

(b) Except to the extent expressly authorized in this Section 9.1 and Sections 9.2, 9.3 and 9.6 below, or as otherwise agreed in writing by the Parties, each Party agrees that, for the Term and for a period of [**] thereafter, it shall (A) keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as expressly provided for in this Agreement any Confidential Information of the other Party (including information relating to this Agreement or the transactions contemplated hereby or the terms hereof), (B) treat the other Party's Confidential Information with the same degree of care the receiving Party uses for its own confidential information but in no event with less than a reasonable degree of care; and (C) reproduce the disclosing Party's Confidential Information solely to the extent necessary or reasonably useful to accomplish the receiving Party's obligations under this Agreement or exercise the receiving Party's rights to use and disclose such Confidential Information as expressly provided for in this Agreement, with all such reproductions being considered the disclosing Party's Confidential Information, provided that, with respect to BMS Confidential Information that was received as confidential information from [**], the obligations of confidentiality and nonuse shall continue until BMS has obtained [**] written consent that the same may be freely used. Notwithstanding anything to the contrary in this Section 9.1, and subject to Section 8.3, the receiving Party may disclose the disclosing Party's Confidential Information to its employees, consultants, agents or permitted (sub)licensees solely on a need-to-know basis for the purpose of fulfilling the receiving Party's obligations under this Agreement or exercising the receiving Party's rights to use and disclose such Confidential Information as expressly provided for in this Agreement; provided, however, that (1) any such employees, consultants, agents or permitted (sub)licensees are bound by obligations of confidentiality and non-use at least as restrictive as those set forth in this Agreement, and (2) the receiving Party remains liable for the compliance of such employees, consultants, agents or permitted (sub)licensees with such obligations. Each receiving Party acknowledges that in connection with its and its representatives examination of the Confidential Information of the disclosing Party, the receiving Party and its representatives may have access to material, non-public information, and that the receiving Party is aware, and will advise its representatives who are informed as to the matters that are the subject of this Agreement, that State and Federal laws, including United States securities laws, may impose restrictions on the dissemination of such information and trading in securities when in possession of such information. Each receiving Party agrees that it will not, and will advise its representatives who are informed as to the matters that are the subject of this Agreement to not, purchase or sell any security of the disclosing Party on the basis of the Confidential Information to the extent such Confidential Information constitute material nonpublic information about the disclosing Party or such security.

(c) Combined Therapy Study Data shall be treated as Confidential Information of each Party and shall not be disclosed to Third Parties except to the extent it falls within the exceptions set forth in Section 9.2 below, is authorized under this Section 9.1 or Section 9.3, is required to be filed with a Regulatory Authority or included in a product's label or package insert, is reasonably necessary to be disclosed in order for a Party to exercise its rights under Section 8.3(b) or 8.3(c) or it is disclosed pursuant to Section 9.5.

9.2 Exceptions. The obligations in Section 9.1 shall not apply with respect to any portion of Confidential Information that the receiving Party can demonstrate by contemporaneous tangible records or other competent proof:

(a) was already known to the receiving Party (or its Affiliates), other than under an obligation of confidentiality, either (i) at the time of disclosure by the disclosing Party, or (ii) if applicable, at the time that it was generated hereunder, whichever ((i) or (ii)) is earlier;

(b) was generally available to the public or otherwise part of the public domain either (i) at the time of its disclosure to the receiving Party, or (ii) if applicable, at the time that it was generated hereunder, whichever ((i) or (ii)) is earlier;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party in breach of this Agreement;

(d) was disclosed to the receiving Party (or its Affiliates), other than under an obligation of confidentiality, by a Third Party who had no obligation to the Party owning or Controlling the information not to disclose such information to others; or

(e) was independently discovered or developed by the receiving Party (or its Affiliates) without the use of, or reference to, the Confidential Information belonging to the disclosing Party.

9.3 Authorized Disclosure. Notwithstanding any other provision of this Agreement, each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary in the following instances:

(a) filing or prosecuting Patent Rights pursuant to Section 6.1(c);

(b) prosecuting or defending litigation;

(c) complying with Applicable Law or the rules or regulations of any securities exchange on which such Party's stock is listed;

(d) disclosure, in connection with the performance of this Agreement, to Affiliates, permitted (sub)licensees, contractors, IRBs, CROs, academic institutions, consultants, agents, investigators, and employees and contractors engaged by study sites and investigators involved with the Combined Therapy Clinical Trial, each of whom prior to disclosure must be bound by terms of confidentiality and non-use at least as protective of Confidential Information as those set forth in this Article 9;

(e) disclosure of the Combined Therapy Study Data, Combined Therapy Inventions and Combined Therapy Patent Rights to Regulatory Authorities in connection with the development of the Combined Therapy, the Recipient Study Drug or the BMS Study Drug;

(f) disclosure of relevant safety information contained within the Combined Therapy Study Data to investigators, IRBs and/or ethics committees and Regulatory Authorities that are involved in other clinical trials of the Recipient Study Drug with respect to the Recipient, and the BMS Study Drug with respect to BMS, and, in the event of a Material Safety Issue, to Third Parties that are collaborating with the Recipient or BMS, respectively in the conduct of such other clinical trials of the Recipient Study Drug or the BMS Study Drug, in each case solely to the extent necessary for the conduct of such clinical trials and/or to comply with Applicable Law and regulatory requirements; and

(g) disclosure (i) to actual and/or bona fide potential licensees and/or collaborators of the terms of this Agreement and (ii) actual and/or bona fide potential acquirers, merger partners, and/or investors, of the Combined Therapy Study Data and the terms of this Agreement, in each case, under confidentiality and non-use obligations at least as protective of Confidential Information as those of this Agreement.

Notwithstanding the foregoing, if a Party is required or otherwise intends to make a disclosure of any other Party's Confidential Information pursuant to Section 9.3(b) and/or Section 9.3(c), it shall give advance notice to such other Party of such impending disclosure and endeavor in good faith to secure confidential treatment of such Confidential Information and/or reasonably assist the Party that owns such Confidential Information in seeking a protective order or other confidential treatment.

9.4 [**].

9.5 Press Releases and Publications.

(a) The Parties shall jointly agree to the content and timing of all public communications with respect to this Agreement (except for the initial press release(s) announcing this Agreement which are attached hereto as Appendix B), subsequent press releases, Q&As, and the content of, and wording for, any listing the Combined Therapy Clinical Trial required to be listed on a public database or other public registry

such as www.clinicaltrials.gov). For clarity, if either Party terminates this Agreement pursuant to Section 12.4, the Parties shall mutually agree upon any external communication related to such termination, which shall not include the rationale for such termination unless (and to the extent) mutually agreed by the Parties; provided that either Party shall be permitted to publicly disclose information that such Party determines in good faith is necessary to be disclosed to comply with Applicable Law or the rules or regulations of any securities exchange on which such Party's stock may be listed, or pursuant to an order of a court or governmental entity.

(b) The Recipient and BMS agree to collaborate to publicly disclose, publish or present (i) top-line results from the Combined Therapy Clinical Trial, limited if possible to avoid jeopardizing the future publication of the Study Data at a scientific conference or in a scientific journal, solely for the purpose of disclosing, as soon as reasonably practicable, the safety or efficacy results and conclusions that are material to either Party under applicable securities laws, and (ii) the conclusions and outcomes (the "Results") of the Combined Therapy Clinical Trial at a scientific conference as soon as reasonably practicable following the completion of such Combined Therapy Clinical Trial, subject in the case of (ii) to the following terms and conditions. The Party proposing to disclose, publish or present the Results shall deliver to the other Party a copy of the proposed disclosure, publication or presentation at least [**] before submission to a Third Party. The reviewing Party shall determine (i) whether information related to its Study Drug is reported and described in medically and scientifically accurate manner and whether this information should be modified or deleted (ii) whether any of its Confidential Information that may be contained in such disclosure, publication or presentation should be modified or deleted and (iii)whether to file a patent application on any Recipient Study Invention (solely with respect to the Recipient) or BMS Study Invention (solely with respect to BMS) or Combined Therapy Invention disclosed therein. The disclosure, publication or presentation shall be delayed for an additional [**] (i.e., a total of [**] from the initial proposal) if the reviewing Party reasonably requests such extension to allow time for the preparation and filing of relevant patent applications. If the reviewing Party reasonably requests modifications to the disclosure, publication or presentation to prevent the disclosure of Confidential Information of the reviewing Party (other than the Results or Study Data) or to correct the medical or scientific accuracy of information associated with its Study Drug (other than the Results or Study Data), the publishing Party shall edit such publication to prevent the disclosure of such information or correct inaccurate medical or scientific information prior to submission of the disclosure, publication or presentation. In the event of a disagreement as to content, timing and/or venue or forum for any disclosure, publication or presentation of the Results, such dispute (a "Publication Dispute") shall be referred to the Executive Officers (or their respective designees); provided that, in the absence of agreement after such good faith discussions, and upon expiration of the additional [**], (A) academic collaborators or clinical trial sites engaged by the Recipient in connection with the performance of the Combined Therapy Clinical Trial may publish Combined Therapy Study Data obtained by such academic collaborator or clinical trial site solely to the extent that such ability to publish such Combined Therapy Study Data is set forth in an agreement between the Recipient and such academic collaborator or clinical trial site relating to the conduct of Combined Therapy Clinical Trial and (B) the publishing Party may proceed with the disclosure, publication or presentation provided that such disclosure, publication or presentation is consistent with its internal publication guidelines and customary industry practices for the publication of similar data and does not disclose the Confidential Information of the other Party (other than the Results or Study Data). Authorship of any publication shall be determined based on the accepted standards used in peer-reviewed academic journals at the time of the proposed disclosure, publication or presentation. The Parties agree that they shall make reasonable efforts to prevent publication of a press release that could jeopardize the future publication of Study Data at a scientific conference or in a scientific journal but in no way will this or any other provision of this Agreement supersede the requirements of any Applicable Law or the rules or regulations of any securities exchange or listing entity on which a Party's stock is listed (including any such rule or regulation that may require a Party to make public disclosures about interim results of the Combined Therapy Clinical Trial). Notwithstanding the foregoing, nothing herein shall prevent or restrict [**] from making any disclosures of unpublished Study Data disclosed to it by BMS pursuant to Section 9.4 or of the existence of this Agreement, in each case in order for [**] to comply with requirements of Applicable Law, the rules or regulations of any securities exchange or listing entity on which its stock may be traded or pursuant to an order of a court or governmental entity to publicly disclose

the existence of the Agreement and the Study Data, provided that if any such disclosure is made by Ono it will only disclose the minimum amount of information necessary to achieve compliance and will provide the Recipient with reasonable advance notice of such disclosure.

(c) The Recipient agrees to include in all press releases, presentations and publications it makes related to the Combined Therapy Clinical Trial specific mention, if applicable, of the BMS Study Drug and the support and involvement of BMS. BMS agrees to include in all press releases, presentations and publications it makes related to the Combined Therapy Clinical Trial specific mention, if applicable, of the Recipient Study Drug and the support and involvement of the Recipient.

9.6 Compliance with Sunshine Laws.

(a) For purposes of compliance with reporting obligations under Sunshine Laws, as between the Parties, the Recipient represents that it is not, as of the Effective Date, subject to reporting obligations under the Sunshine Laws. Therefore, as between the Parties, BMS will report payments or other transfers of value ("POTV") made by the Recipient or the CRO related to the conduct of the Combined Therapy Clinical Trial and any applicable associated contractor engagements as required under the Sunshine Laws for the Combined Therapy Clinical Trial. BMS shall request delayed publication for any reported POTV for studies sponsored by the Recipient as permitted under the Sunshine Laws and if consistent with BMS's normal business practices. In the event that the Recipient becomes responsible for reporting POTV for studies sponsored by it in a given country during the Term, the Recipient shall provide written notification to BMS and the Parties will meet to confer to discuss how they wish to handle reporting thereafter. Interpretation of the Sunshine Laws for purposes of reporting any POTV by a Party shall be in such Party's sole discretion so long as the interpretation complies with Applicable Law.

(b) The Recipient (i) will provide (to the extent in the possession of the Recipient), or will utilize Commercially Reasonable Efforts to obligate and ensure that each CRO and other applicable Third Party contractors for the Combined Therapy Clinical Trial provides, BMS with any information requested by BMS as BMS may reasonably determine is necessary for BMS to comply with its reporting obligations under Sunshine Laws (with such amounts paid to, or at the direction of, healthcare providers, teaching hospitals and/or any other persons for whom POTVs must be reported under Sunshine Laws to be reported to BMS within a reasonable time period specified by BMS) and (ii) will reasonably cooperate with, and will utilize Commercially Reasonable Efforts to obligate and ensure that each CRO and other applicable Third Party contractors for the Combined Therapy Clinical Trial reasonably cooperates with, BMS in connection with its compliance with such Sunshine Laws. The form in which the Recipient provides any such information shall be mutually agreed but sufficient to enable BMS to comply with its reporting obligations and BMS may disclose any information that it believes is necessary to comply with Sunshine Laws. Without limiting the foregoing, BMS shall have the right to allocate POTVs in connection with this Agreement in any required reporting under Sunshine Laws in accordance with its normal business practices. These obligations shall survive the expiration and termination of this Agreement to the extent necessary for BMS to comply with Sunshine Laws. The Recipient shall not be required to provide any information to BMS that is subject to disclosure pursuant to the Recipient's own obligations under the Sunshine Laws.

(c) For purposes of this Section 9.6, "Sunshine Laws" shall mean Applicable Laws requiring collection, reporting and disclosure of POTVs to certain healthcare providers, entities and individuals. These Applicable Laws may include relevant provisions of the Patient Protection and Affordable Health Care Act of 2010 and implementing regulations thereunder.

9.7 Destruction of Confidential Information. Upon expiration or termination of the Agreement, the receiving Party shall, upon request by the other Party, immediately destroy or return all of the other Party's Confidential Information relating solely to its Study Drug as monotherapy (but not to the Combined Therapy or the Combined Therapy Study Data) in its possession; provided, however, that the receiving Party shall be entitled to retain one (1) copy of Confidential Information solely for record-keeping purposes and shall not be required to destroy any Confidential Information required, or reasonably necessary, to be retained

for any clinical trial activities that continue after expiration or termination, or off-site computer files created during automatic system back up which are subsequently stored securely by the receiving Party.

ARTICLE 10

REPRESENTATIONS AND WARRANTIES

10.1 Authority and Binding Agreement. Each Party represents and warrants to the other Party that (a) it has the corporate power and authority and the legal right to enter into this Agreement and perform its obligations hereunder, (b) it has taken all necessary corporate action on its part required to authorize the execution and delivery of the Agreement and the performance of its obligations hereunder, and (c) the Agreement has been duly executed and delivered on behalf of such Party and constitutes a legal, valid and binding obligation of such Party that is enforceable against it in accordance with its terms subject to bankruptcy, insolvency, reorganization, arrangement, winding-up, moratorium, and similar laws of general application affecting the enforcement of creditors' rights generally, and subject to general equitable principles, including the fact that the availability of equitable remedies, such as injunctive relief or specific performance, is in the discretion of the court.

10.2 No Conflicts. Each Party represents and warrants to the other Party that, to the best of its knowledge, it has not entered, and shall not enter, into any agreement with any Third Party that is in conflict with the rights granted to the other Party under this Agreement, and has not taken any action that would in any way prevent it from granting the rights granted to the other Party under this Agreement, or that would otherwise materially conflict with or adversely affect the rights granted to the other Party under this Agreement.

10.3 Litigation. Each Party represents and warrants to the other Party, to the best of its knowledge, it is not aware of any pending or threatened litigation (and has not received any communication) that alleges that its activities related to this Agreement have violated, or that by conducting the activities as contemplated in this Agreement it would violate, any of the intellectual property rights of any other Person (after giving effect to the license grants in this Agreement).

10.4 No Adverse Proceedings. Each Party represents and warrants to the other Party that, except as otherwise notified to the other Party, there is not pending or, to the knowledge of such Party, threatened, against such Party, any claim, suit, action or governmental proceeding that would, if adversely determined, materially impair the ability of such Party to perform its obligations under this Agreement.

10.5 Consents. Each Party represents and warrants to the other Party that, to the best of its knowledge, all necessary consents, approvals and authorizations of all regulatory and governmental authorities and other Persons (a) required to be obtained by such Party in connection with the execution and delivery of this Agreement have been obtained (or will have been obtained prior to such execution and delivery) and (b) required to be obtained by such Party in connection with the performance of its obligations under this Agreement have been obtained or will be obtained prior to such performance.

10.6 No Debarment. Each Party hereby certifies to the other that it has not used, and will not use the services of any person disqualified, debarred, banned, subject to debarment or convicted of a crime for which a person could be debarred by the FDA under 21 U.S.C. 335a, as amended (or subject to a similar sanction of any other Regulatory Authority), in any capacity in connection with any of the services or work provided under the Combined Therapy Clinical Trial and that this certification may be relied upon in any applications to the FDA or any other Regulatory Authority. It is understood and agreed that this certification imposes a continuing obligation upon each Party to notify the other promptly of any change in the truth of this certification. Upon request by a Party, the other Party agrees to provide a list of persons used to perform the services or work provided under any activities conducted for or on behalf of such Party or any of its Affiliates pursuant to this Agreement who, within the [**] preceding the Effective Date, or subsequent to the Effective Date, were or are convicted of one of the criminal offenses required by 21 U.S.C. 335a, as amended, to be listed in any application for approval of an abbreviated application for drug approval.

10.7 Compliance with Applicable Law. Each Party represents and warrants to the other Party that it shall comply with all Applicable Law of the country or other jurisdiction, or any court or agency thereof, applicable to the performance of its activities hereunder or any obligation or transaction hereunder, including those pertaining to the production and handling of drug products, such as those set forth by the Regulatory Authorities, as applicable, and the applicable terms of this Agreement in the performance of its obligations hereunder.

10.8 Affiliates. Each Party represents and warrants to the other Party that, to the extent the intellectual property, Regulatory Documentation or Technology licensed by it hereunder are Controlled by its Affiliates or a Third Party, it has the right to use, and has the right to grant (sub)licenses to the other Party to use, such intellectual property, Regulatory Documentation or Technology in accordance with the terms of this Agreement.

10.9 Ethical Business Practices. Each Party represents and warrants to the other Party that neither it nor its Affiliates will make any payment, either directly or indirectly, of money or other assets, including the compensation such Party derives from this Agreement (collectively a "Payment"), to government or political party officials, officials of International Public Organizations, candidates for public office, or representatives of other businesses or persons acting on behalf of any of the foregoing (collectively "Officials") where such Payment would constitute violation of any law, including the Foreign Corrupt Practices Act of 1977, 15 U.S.C. §§ 78dd-1, et seq. In addition, regardless of legality, neither it nor its Affiliates will make any Payment either directly or indirectly to Officials if such Payment is for the purpose of improperly influencing decisions or actions with respect to the subject matter of this Agreement. All activities will be conducted in compliance with the U.S. False Claims Act and the U.S. Anti-Kickback Statute.

10.10 Accounting. Each Party represents and warrants to the other Party that all transactions under the Agreement shall be properly and accurately recorded in all material respects on its books and records and that each document upon which entries in such books and records are based is complete and accurate in all material respects.

10.11 Single Agent Study Drug Safety Issues. Each Party represents and warrants that, to the best of its knowledge, it is not aware of any material safety or toxicity issue with respect to its Single Agent Study Drug that are not reflected in the investigator's brochure for its Single Agent Study Drug existing as of the Effective Date.

10.12 Compliance with Licensor Agreements. Each Party will use, and will cause its Affiliates to use, Commercially Reasonable Efforts to comply with its obligations under any agreements entered into by it or its Affiliates with a Third Party under which it is licensed any intellectual property rights or confidential information relating to a Study Drug (and not to voluntarily terminate same) to the extent necessary for the Combined Therapy Clinical Trial to be conducted and completed in accordance with the terms of this Agreement and for the other Party to receive the rights and benefits provided to it under this Agreement.

10.13 DISCLAIMER OF WARRANTY. THE EXPRESS REPRESENTATIONS AND WARRANTIES STATED IN THIS ARTICLE 10 ARE IN LIEU OF, AND THE PARTIES DO HEREBY DISCLAIM, ALL OTHER REPRESENTATIONS AND WARRANTIES, EXPRESS, IMPLIED OR STATUTORY, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE OR USE, AND NON-INFRINGEMENT OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS.

ARTICLE 11

INDEMNIFICATION

11.1 BMS Indemnification. BMS hereby agrees to defend, hold harmless and indemnify (collectively, "Indemnify") the Recipient, its Affiliates, and its and their agents, directors, officers, employees and subcontractors (the "Recipient Indemnitees") from and against any and all liabilities, expenses and/or losses,

including reasonable legal expenses and attorneys' fees (collectively "Losses") resulting from Third Party suits, claims, actions and demands (each, a "Third Party Claim") to the extent that they arise or result from (a) the negligence or intentional misconduct of any BMS Indemnitee or any (sub)licensee of BMS conducting activities on behalf of BMS under this Agreement, (b) any breach by BMS of any provision of this Agreement, (c) any injury (other than resulting from known adverse effects) to a subject in the Combined Therapy Clinical Trial to the extent caused solely by the BMS Study Drug, or (d) the use by BMS, its Affiliates, contractors or (sub)licensees of Combined Therapy Study Data, BMS Study Data, BMS Study Inventions, BMS Study Patent Rights, Combined Therapy Inventions and Combined Therapy Patent Rights (other than with respect to Third Party Claims that are covered under Section 6.4); but excluding, in each case ((a) through (d)), any such Losses to the extent arising or resulting from a cause or event for which the Recipient is obligated to Indemnify the BMS Indemnitees pursuant to Section 11.2.

11.2 Recipient Indemnification. The Recipient hereby agrees to Indemnify BMS, its Affiliates, and its and their agents, directors, officers, employees and subcontractors (the "BMS Indemnitees") from and against any and all Losses resulting from Third Party Claims to the extent that they arise or result from (a) the negligence or intentional misconduct of any Recipient Indemnitee or any (sub)licensee of the Recipient conducting activities on behalf of the Recipient under this Agreement, (b) any breach by the Recipient of any provision of this Agreement, (c) any injury to a subject in the Combined Therapy Clinical Trial, or (d) the use by the Recipient, its Affiliates, contractors or (sub)licensees of Combined Therapy Study Data, Recipient Study Data, Recipient Study Inventions, Recipient Study Patent Rights, Combined Therapy Inventions and Combined Therapy Patent Rights (other than with respect to Third Party Claims that are covered under Section 6.4); but excluding, in each case ((a) through (d)), any such Losses to the extent arising or resulting from a cause or event for which BMS is obligated to Indemnify the Recipient Indemnitees pursuant to Section 11.1.

11.3 Indemnification Procedure. Each Party's agreement to Indemnify the other Party is conditioned on the performance of the following by the Party seeking indemnification: (a) providing written notice to the Indemnifying Party of any Loss and/or Third Party Claim of the types set forth in Section 11.1 and 11.2 promptly, and in any event within [**], after the Party seeking indemnification has knowledge of such Loss and/or Third Party Claim; provided that, any delay in complying with the requirements of this clause (a) will only limit the Indemnifying Party's obligation to the extent of the prejudice caused to the Indemnifying Party by such delay, (b) permitting the Indemnifying Party to assume full responsibility to investigate, prepare for and defend against any such Loss and/or Third Party Claim, (c) providing reasonable assistance to the Indemnifying Party, at the Indemnifying Party's expense, in the investigation of, preparation for and defense of any Loss and/or Third Party Claim, and (d) not compromising or settling such Loss and/or Third Party Claim without the Indemnifying Party's written consent, such consent not to be unreasonably withheld or delayed.

11.4 Separate Defense of Claims. In the event that the Parties cannot agree as to the application of Sections 11.1 and/or 11.2 to any particular Loss, the Parties may conduct separate defenses of such Loss. Each Party further reserves the right to claim indemnity from the other in accordance with Sections 11.1 and/or 11.2 upon resolution of the underlying claim, notwithstanding the provisions of Section 11.3(b).

Insurance. Each Party shall maintain commercially reasonable levels of insurance or other adequate and commercially reasonable forms of protection or self-insurance to satisfy its indemnification obligations under this Agreement. Each Party shall provide the other Party with written notice at least [**] prior to the cancellation, non-renewal or material change in such insurance or self- insurance which would materially adversely affect the rights of the other Party hereunder. The maintenance of any insurance shall not constitute any limit or restriction on damages available to a Party under this Agreement.

11.5 LIMITATION OF LIABILITY. NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY FOR INDIRECT, INCIDENTAL, CONSEQUENTIAL OR SPECIAL DAMAGES, INCLUDING LOST PROFITS, ARISING FROM OR RELATING TO THIS AGREEMENT AND/OR SUCH PARTY'S PERFORMANCE HEREUNDER, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH

DAMAGES AND REGARDLESS OF THE CAUSE OF ACTION (WHETHER IN CONTRACT, TORT, BREACH OF WARRANTY OR OTHERWISE). NOTHING IN THIS SECTION 11.6 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF A PARTY UNDER SECTIONS 11.1 OR 11.2 IN RELATION TO, OR DAMAGES AVAILABLE FOR, BREACHES OF CONFIDENTIALITY OBLIGATIONS IN ARTICLE 9 OR FOR A PARTY'S GROSS NEGLIGENCE OR WILLFUL MISCONDUCT.

ARTICLE 12

TERM AND TERMINATION

12.1 Term. This Agreement shall be effective as of the Effective Date and, unless earlier terminated pursuant to Sections 12.2, 12.3 or 12.4 or any other termination right expressly stated in this Agreement, shall continue in effect until completion of the Combined Therapy Clinical Trial by all centers participating in the Combined Therapy Clinical Trial, delivery of all Study Data, including all completed case report forms, all final analyses and all final clinical study reports contemplated by the Combined Therapy Clinical Trial to both Parties, and the completion of any statistical analyses and bioanalyses contemplated by the Protocol or otherwise agreed to by the Parties to be conducted under this Agreement (the "Term").

12.2 Termination for Material Breach.

(a) Notice and Cure Period. If a Party (the "Breaching Party") is in material breach of its obligations under this Agreement, the other Party (the "Non-Breaching Party") shall have the right to give the Breaching Party notice specifying the nature of such material breach. The Breaching Party shall have a period of [**] after receipt of such notice to cure such material breach (the "Cure Period") in a manner reasonably acceptable to the Non-Breaching Party. For the avoidance of doubt, this provision is not intended to restrict in any way either Party's right to notify the other Party of any other breach or to demand the cure of any other breach.

(b) Termination Right. The Non-Breaching Party shall have the right to terminate this Agreement, upon written notice, in the event that the Breaching Party has not cured such material breach within the Cure Period, provided, however, that if such breach is capable of cure but cannot be cured within the Cure Period, and the Breaching Party commences actions to cure such material breach within the Cure Period and thereafter diligently continue such actions, the Breaching Party shall have an additional [**] to cure such breach. If a Party contests such termination pursuant to the dispute resolution procedures under Section 13.3, such termination shall not be effective until a conclusion of the dispute resolution procedures in Section 13.3, as applicable, resulting in a determination that there has been a material breach that was not cured within the Cure Period (which Cure Period shall be tolled for the period from notice of such dispute until resolution of such dispute pursuant to Section 13.3 or abandonment of such dispute by the disputing Party).

12.3 Termination for Bankruptcy. Either Party may terminate this Agreement if, at any time, the other Party shall file in any court or agency pursuant to any statute or regulation of any state, country or jurisdiction, a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of such other Party or of such other Party's assets, or if the other Party proposes a written agreement of composition or extension of its debts, or if the other Party shall be served with an involuntary petition against it, filed in any insolvency proceeding, and such petition shall not be dismissed or stayed within [**] after the filing thereof, or if the other Party will propose or be a party to any dissolution or liquidation, or if the other Party shall make an assignment for the benefit of its creditors.

12.4 Termination due to Material Safety Issue; Clinical Hold.

(a) Either Party shall have the right to terminate this Agreement [**] (after meeting and discussing with the other Party in good faith as described in the following sentence) upon written notice if it deems it necessary to protect the safety, health or welfare of subjects enrolled in the Combined Therapy

Clinical Trial due to the existence of a Material Safety Issue. In the event of a termination due to a Material Safety Issue, prior to the terminating Party providing written notice, each Party's safety committee shall, to the extent practicable, meet and discuss in good faith the safety concerns raised by the terminating Party and consider in good faith the input, questions and advice of the non- terminating Party, but should any dispute arise in such discussion, the dispute resolution processes set forth in Section 13.3 shall not apply to such dispute and the terminating Party shall have the right to issue such notice and such termination shall take effect without the Parties first following the procedures set forth in Section 13.3.

(b) If a Clinical Hold with respect to either the BMS Study Drug or the Recipient Study Drug should arise at any time after the Effective Date, the Parties will meet and discuss the basis for the Clinical Hold, how long the Clinical Hold is expected to last, and how they might address the issue that caused the clinical hold. If, after [**] of discussions following the Clinical Hold, either Party reasonably concludes that the issue adversely impacts the Combined Therapy Clinical Trial and is not solvable or that unacceptable and material additional costs/delays have been and/or will continue to be incurred in the conduct of the Combined Therapy Clinical Trial, then such Party may immediately terminate this Agreement.

12.5 Effect of Termination. Upon expiration or termination of this Agreement, (a) the licenses granted to the Recipient to conduct the Combined Therapy Clinical Trial in Section 3.1 (and any sublicenses granted under Section 3.2) shall terminate, and (b) the Parties shall use reasonable efforts to wind down activities under this Agreement in a reasonable manner and avoid incurring any additional expenditures or non- cancellable obligations; provided that, in the case of termination pursuant to Section 12.4, the Recipient may continue to dose subjects enrolled in the Combined Therapy Clinical Trial through completion of the Protocol if dosing is required by the applicable Regulatory Authority(ies) and/or Applicable Law. Any such wind-down activities will include the return to BMS, or destruction, of all BMS Study Drug provided to the Recipient and not consumed in the Combined Therapy Clinical Trial, except in the event that the Recipient terminates this Agreement pursuant to Section 12.2 or 12.3, in which case the Recipient shall continue to have the right to use any BMS Study Drug provided to Recipient for the conduct of the Combined Therapy Clinical Trial.

12.6 Survival. The following Articles and Sections of this Agreement and all definitions relating thereto shall survive any expiration or termination of this Agreement for any reason: Section 6.1(b), Section 2.4, Section 4.5, Sections 5.1(e)-(h), Section 5.1(j), Section 5.1(k), Section 5.1(o), Article 6 ("Intellectual Property"), Article 7 ("Costs and Expenses), Article 8 ("Records and Study Data"), Article 9 ("Confidentiality"); Article 10 ("Representations and Warranties"), Article 11 ("Indemnification"), Section 12.5 ("Effect of Termination"), Section 12.6 ("Survival"), Section 13.1 ("Entire Agreement"), Section 13.2 ("Governing Law"), Section 13.3 ("Dispute Resolution"), Section 13.4 ("Injunctive Relief"), Section 13.6 ("Notices"), Section 13.7 ("No Waiver, Modifications"), Section 13.8 ("No Strict Construction"), Section 13.9 ("Independent Contractor"), Section 13.10 ("Assignment, Licenses"), Section 13.11 ("Headings"), Section 13.13 ("Severability"), Section 13.15 ("No Benefit to Third Parties"), and Section 13.16 ("Construction").

ARTICLE 13

MISCELLANEOUS

13.1 Entire Agreement. The Parties acknowledge that this Agreement shall govern all activities of the Parties with respect to the Combined Therapy Clinical Trial from the Effective Date forward. This Agreement, including the Exhibits hereto and together with the Supply and Quality Documentation, sets forth the complete, final and exclusive agreement between the Parties concerning the subject matter hereof and supersedes all prior agreements and understandings between the Parties with respect to such subject matter. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties with respect to such subject matter other than as are set forth in this Agreement. All Exhibits attached hereto are incorporated herein as part of this Agreement.

13.2 Governing Law. This Agreement shall be governed and construed in accordance with the internal laws of the State of Delaware, USA, excluding any choice of law rules that may direct the application of the laws of another jurisdiction.

13.3 Dispute Resolution.

(a) The Parties' Designated Clinical Contacts (for clinical and regulatory matters) and the Parties Designated Supply Contacts (for supply matters) shall attempt in good faith to resolve any dispute or concern that either Party may bring to the other Party's attention.

(b) In the event of any dispute, controversy or claim arising out of, relating to or in connection with any provision of this Agreement (each a "Dispute"), other than a Publication Dispute or a dispute as to whether a Material Safety Issue exists, that cannot be resolved by the applicable Designated Contacts of each Party, then upon the request of either Party by written notice, the Parties shall refer such Dispute to the Executive Officers. This Agreement shall remain in effect during the pendency of any such dispute. In the event that no resolution is made by the Executive Officers (or their designee) in good faith negotiations within [**] after such referral to them, then:

(i) if such Dispute constitutes an Arbitration Matter, such Dispute shall be resolved through arbitration in accordance with the remainder of this Section 13.3; provided, however, that with respect to any such Dispute that relates to a matter described in Section 13.4, either Party shall have the right to seek an injunction or other equitable relief without waiting for the expiration of such [**];

(ii) if such Dispute constitutes a Publication Dispute, the specific dispute resolution processes contained in Section 9.6(b) will apply; and

(iii) if such Dispute regards the supply, quality or compliance with specifications of the Recipient Study Drug, the Dispute will be resolved by the Recipient; provided that (A) the Recipient shall have no authority to amend, change or waive compliance with this Agreement, which matters may be approved only by the written consent of both Parties, (B) all determinations made by the Recipient shall be consistent with the terms of this Agreement, and (C) any disputes relating to the supply, quality or compliance with specifications of the BMS Study Drug shall be the responsibility of BMS.

(c) If a Dispute that constitutes an Arbitration Matter remains unresolved after escalation to the Executive Officers as described above, either Party may refer the matter to arbitration as described herein. Any arbitration under this Agreement shall be conducted under the auspices of the American Arbitration Association by a panel of three (3) arbitrators pursuant to that organization's Commercial Arbitration Rules then in effect. The fees and expenses of the arbitrators shall be borne in equal shares by the Parties. Each Party shall bear the fees and expenses of its legal representation in the arbitration. The arbitral tribunal shall not reallocate either the fees and expenses of the arbitrators or of the Parties' legal representation. The arbitration shall be held in New York, New York, USA, which shall be the seat of the arbitration. The language of the arbitration shall be English.

13.4 Injunctive Relief. Notwithstanding anything herein to the contrary, a Party may seek an injunction or other injunctive relief from any court of competent jurisdiction in order to prevent immediate and irreparable injury, loss or damage on a provisional basis. For the avoidance of doubt, if either Party (a) discloses Confidential Information of the other Party other than as permitted under Article 9, (b) uses (in the case of the Recipient) the BMS Study Drug or BMS Technology or (in the case of BMS) the Recipient Study Drug or Recipient Technology in any manner other than as expressly permitted under this Agreement or (c) otherwise is in material breach of this Agreement and such material breach could cause immediate harm to the value of the Recipient Study Drug (if BMS is in material breach) or the BMS Study Drug (if the Recipient is in material breach), the other Party shall have the right to seek an injunction or other equitable relief precluding the other Party from continuing its activities related to the Combined Therapy Clinical Trial without waiting for the conclusion of the dispute resolution procedures under Section 13.3.

13.5 Force Majeure. The Parties shall be excused from the performance of their obligations under this Agreement (other than the payment of monies owed to the other Party) to the extent that such performance is prevented by force majeure and the non-performing Party promptly provides notice of the prevention to the other Party. Such excuse shall be continued so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. For purposes of this Agreement, force majeure shall mean acts of God, strikes or other concerted acts of workers, civil disturbances, fires, earthquakes, acts of terrorism, floods, explosions, riots, war, rebellion, sabotage or failure or default of public utilities or common carriers or similar conditions beyond the control of the Parties.

13.6 Notices. Any notice required or permitted to be given under this Agreement shall be in writing, shall specifically refer to this Agreement and shall be deemed to have been sufficiently given for all purposes if such notice is timely and is: (a) mailed by first class certified or registered mail, postage prepaid, return receipt requested, (b) sent by express delivery service, or (c) personally delivered. Unless otherwise specified in writing, the mailing addresses of the Parties shall be as described below.

For the Recipient: AVEO Pharmaceuticals, Inc.
30 Winter Street
Boston, MA 02108
Attention: Chief Executive Officer

With a copy to: AVEO Pharmaceuticals, Inc.
30 Winter Street
Boston, MA 02108 Attention: Legal Department

For BMS: Bristol-Myers Squibb Company Route 206 and
Province Line Road Princeton, NJ 08543-4000
Attention: VP, Business Development

With a copy to: Bristol-Myers Squibb Company
Route 206 and Province Line Road Princeton, NJ 08543-4000
Attention: VP & Assistant General Counsel, Business Development

Any such communication shall be deemed to have been received when delivered. It is understood and agreed that this Section 13.6 is not intended to govern the day-to-day business communications necessary between the Parties in performing their duties, in due course, under the terms of this Agreement.

13.7 No Waiver; Modifications. It is agreed that no waiver by a Party hereto of any breach or default of any of the covenants or agreements herein set forth shall be deemed a waiver as to any subsequent and/or similar breach or default. No amendment, modification, release or discharge shall be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

13.8 No Strict Construction. This Agreement has been prepared jointly and shall not be strictly construed against either Party. No presumption as to construction of this Agreement shall apply against either Party with respect to any ambiguity in the wording of any provision(s) of this Agreement irrespective of which Party may be deemed to have authored the ambiguous provision(s).

13.9 Independent Contractor. The Parties are independent contractors of each other, and the relationship between the Parties shall not constitute a partnership, joint venture or agency. Neither Party shall be the agent of the other or have any authority to act for, or on behalf of, the other Party in any matter.

13.10 Assignment; Licensees.

(a) Assignment. Neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other Party, except that a Party may make

such an assignment without the other Party's consent (i) to an Affiliate, (ii) to a Third Party that merges with, consolidates with or acquires substantially all of the assets or voting control of the assigning Party or (iii) to a Third Party that acquires all the rights of the assigning Party to the Recipient Study Drug, in the case of the Recipient, or the BMS Study Drug, in the case of BMS. If assigned or transferred to an Affiliate, the assigning/transferring Party shall remain jointly and severally responsible and liable with the assignee/transferee Affiliate for the assigned rights and/or obligations. If assigned to a Third Party, any permitted successor or assignee of rights and/or obligations hereunder shall, in a writing to the other Party, expressly assume performance of such rights and/or obligations. Any assignment or attempted assignment by any Party in violation of the terms of this Section 13.10(a) shall be null and void and of no legal effect.

(b) Licensees. If a Party grants a third party a license (other than a license solely to make a product for a Party and other than any license rights granted to [**] for the [**], or to [**] for the [**] Territory or to [**] for the [**] Territory) to develop and commercialize its Single Agent Study Drug on a worldwide basis or in any geographic region and/or for all purposes or a limited field, (a "Licensee"), such Party will obtain the Licensee's agreement to abide by the terms of this Agreement in the same manner as the licensing Party.

13.11 Headings. The captions to the several Sections and Articles hereof are not a part of this Agreement, but are included merely for convenience of reference only and shall not affect its meaning or interpretation.

13.12 Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Agreement may be executed by facsimile or electronic (e.g., pdf) signatures and such signatures shall be deemed to bind each Party hereto as if they were original signature.

13.13 Severability. If any provision of this Agreement is held to be illegal, invalid or unenforceable under any present or future law, and if the rights or obligations of a Party under this Agreement will not be materially and adversely affected thereby, (a) such provision shall be fully severable, (b) this Agreement shall be construed and enforced as if such illegal, invalid or unenforceable provision had never comprised a part hereof, (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid or unenforceable provision or by its severance herefrom and (d) in lieu of such illegal, invalid or unenforceable provision, there shall be added automatically as a part of this Agreement a legal, valid and enforceable provision as similar in terms to such illegal, invalid or unenforceable provision as may be possible and reasonably acceptable to the Parties.

13.14 Further Assurance. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary or as the other Party may reasonably request in order to perfect any license, assignment or other transfer or any properties or rights under, or pursuant, to this Agreement.

13.15 No Benefit to Third Parties. The representations, warranties and agreements set forth in this Agreement are for the sole benefit of the Parties and their successors and permitted assigns, and they shall not be construed as conferring any rights on any other parties.

13.16 Construction.

(a) General. Except as otherwise explicitly specified to the contrary, (i) references to a Section, Article or Exhibit means a Section or Article of, or Exhibit to, this Agreement and all subsections thereof, unless another agreement is specified, (ii) references to a particular statute or regulation include all rules and regulations promulgated thereunder and any successor statute, rules or regulations then in effect, in each case including the then-current amendments thereto, (iii) words in the singular or plural form include the plural and singular form, respectively, (iv) the terms "including," "include(s)," "such as," and "for example" used in this Agreement mean including the generality of any description preceding such term and will be deemed to be followed by "without limitation", (v) the words "hereof," "herein," "hereunder,"

"hereby" and derivative or similar words refer to this Agreement, (vi) "or" is used in the conjunctive ("and/or") unless the context requires otherwise, (vii) "will" and "shall" are synonyms, and (viii) days means calendar days. No presumption as to construction of this Agreement shall apply against either Party with respect to any ambiguity in the wording of any provision(s) of this Agreement irrespective of which Party may be deemed to have authored the ambiguous provision(s).

(b) No Response. Except as expressly set forth in this Agreement, where a provision of this Agreement provides for a Party to respond within a designated period following written notice from the other Party, and if such Party fails to respond, then the failure to respond shall not be deemed to create or imply: (i) that the non-responding Party agrees or disagrees with the proposed action to be taken by the other Party, (ii) any amendment, change or waiver of the terms of this Agreement, or (iii) any consent that an action proposed to be taken may be taken if it conflicts with the terms of this Agreement and/or waiver of any rights it may have to seek remedies at law or in equity for breach of this Agreement as a result of the action taken.

[Signature page follows]

IN WITNESS WHEREOF, the Parties, intending to be legally bound hereby, have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

Aveo Pharmaceuticals, Inc.	**Bristol-Myers Squibb Company**
By: /s/ Michael Bailey	By: /s/ Jonathan Cheng
Name: Michael Bailey	Name: Jonathan Cheng
Title: Chief Executive Officer	Title: Head of Oncology Development
Date: 26 Jan 2021	Date: 26 Jan 2021

Exhibit Index

Attached:

Appendix A:	Draft Protocol
Appendix B:	Press Release
Appendix C:	Territory
Appendix D:	[**] Territory
Appendix E:	[**] Territory

Exhibit 10.3

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

AMENDMENT No. 1

to

Clinical Trial Collaboration and Supply Agreement

This Amendment No. 1 to Clinical Trial Collaboration and Supply Agreement (this "***Amendment No. 1***") is effective as of the date signed by the last party to sign below (the "***Amendment No. 1 Effective Date"***) and is made and entered into by and among Aveo Pharmaceuticals, Inc., having a place of business at 30 Winter Street, Boston, MA 02108("***Recipient"***) and Bristol-Myers Squibb Company, having a place of business at Route 206 & Province Line Road, Princeton, New Jersey 08543-4000, New York, New York 10154 ("***BMS***").

RECITALS

WHEREAS, Recipient and BMS entered into that certain Clinical Trial Collaboration and Supply Agreement dated January 26, 2021 (the **"*Agreement"***); and

WHEREAS, Recipient and BMS desire to amend the Agreement to expand the Territorywhere the Combined Therapy Clinical Trial may be conducted.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual promises and covenants contained herein, Recipient and BMS agree as follows:

1. The terms in this Amendment No. 1 with initial letters capitalized, whether used in the singular or the plural, shall have the meaning set forth herein, or if not defined herein, as set forthin the Agreement.

2. *Territory Expansion*. Appendix C of the Agreement is hereby deleted in its entirety and replaced with the revised Appendix C attached hereto as Exhibit A.

3. Except as expressly set forth herein, all provisions of the Agreement shall remain unchanged and in full force and effect.

4. This Amendment No. 1 may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Amendment No. 1 may be executed by facsimile or electronic (e.g., .pdf) signatures and such signatures shall be deemed to bind each party hereto as if they were original signatures.

[Signature page follows]

IN WITNESS WHEREOF, Recipient and BMS, intending to be legally bound hereby, have caused this Amendment No. 1 to be executed by their duly authorized representatives as of the date(s) below.

Aveo Pharmaceuticals, Inc.	**Bristol-Myers Squibb Company**
By: /s/ Michael Bailey	By: /s/ Paul Haluska
Name: Michael Bailey	Name: Paul Haluska
Title: Chief Executive Officer	Title: Head, Clinical Search & Collaborations
Date: 23 March 2021	Date: 25 March 2021

Exhibit 31.1

CERTIFICATION

I, Michael Bailey, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, Inc.;

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 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 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: May 10, 2021

/s/Michael Bailey
Michael Bailey
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Erick Lucera, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, Inc.;

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 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 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: May 10, 2021

/s/Erick Lucera
Erick Lucera
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Michael Bailey, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(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: May 10, 2021

/s/Michael Bailey
Michael Bailey
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of AVEO Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Erick Lucera, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(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: May 10, 2021

/s/Erick Lucera
Erick Lucera
Chief Financial Officer
(Principal Financial Officer)