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, 2022

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 2, 2022: 34,477,715

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References to AVEO

Throughout this Form 10-Q, the words "we," "us," "our" and "AVEO", except where the context requires otherwise, refer to AVEO Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of AVEO Pharmaceuticals, Inc.

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 commercialize FOTIVDA;
- our manufacturing, marketing and sales capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our products;
- our plans to develop our clinical stage assets and commercialize our product candidates;
- 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;
- 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;
- impacts resulting from the COVID-19 pandemic and responsive actions relating thereto;
- 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;
- our intellectual property position;
- 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 II 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 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 quarterly 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 II 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.
- If we fail to comply with the covenants or payment obligations under the 2020 Loan Facility, which could result in an event of default, this could materially and adversely affect our business and our financial condition.
- We have only recently transitioned from a development stage biopharmaceutical company to a commercial 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 commercial product, FOTIVDA, and on our clinical stage assets, including tivozanib (in other indications), ficlatuzumab, AV-380 and AV-203. 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.
- The COVID-19 pandemic has adversely disrupted our ability to commercialize FOTIVDA, to manufacture clinical product, and to initiate new trials or complete ongoing clinical trials and may have other adverse effects on our business and operations.
- 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 the countries in the EUSA Licensed Territory 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 from the EUSA Licensed Territory.

- Any failure by a third-party manufacturer or a third-party supplier to timely produce or provide required manufacturing supplies for us or to safely store product candidate supplies and commercial supplies of FOTIVDA may delay or impair our ability to manufacture product, initiate or complete our clinical trials or commercialize our product candidates.

- 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.

Part I. **Financial Information**

AVEO PHARMACEUTICALS, INC.

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

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 73,846	$ 70,542
Marketable securities	5,192	16,784
Trade receivables, net	12,943	9,811
Partnership receivables	831	1,790
Inventory	1,694	1,656
Clinical trial retainers	734	1,181
Other prepaid expenses and other current assets	2,486	2,972
Total current assets	97,726	104,736
Property and equipment, net	259	276
Operating lease right-of-use asset	130	178
Other assets	100	151
Total assets	$ 98,215	$ 105,341
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,014	$ 2,712
Accrued clinical trial costs and contract research	6,772	5,046
Accrued compensation and benefits	3,469	4,963
Other accrued liabilities	7,041	5,421
Operating lease liability	8	11
Deferred revenue	—	578
Total current liabilities	20,304	18,731
Loans payable, net of discount	38,189	37,960
Other liabilities, non-current (Note 6)	2,780	2,780
Total liabilities	61,273	59,471
Stockholders' equity:		
Preferred stock, $.001 par value: 5,000 shares authorized at March 31, 2022 and December 31, 2021; no shares issued and outstanding at each of March 31, 2022 and December 31, 2021	—	—
Common stock, $.001 par value: 50,000 shares authorized at March 31, 2022 and December 31, 2021; 34,475 shares issued and outstanding at March 31, 2022 and December 31, 2021	34	34
Additional paid-in capital	721,653	720,386
Accumulated other comprehensive gain/(loss)	1	(3)
Accumulated deficit	(684,746)	(674,547)
Total stockholders' equity	36,942	45,870
Total liabilities and stockholders' equity	$ 98,215	$ 105,341

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

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

	Three Months Ended March 31,	
	2022	**2021**
Revenues:		
FOTIVDA U.S. product revenue, net	$ 20,086	$ 1,066
Partnership licensing and royalty revenue	834	854
	20,920	1,920
Operating expenses:		
Cost of products sold	2,434	138
Research and development	10,160	5,797
Selling, general and administrative	17,337	15,100
	29,931	21,035
Loss from operations	(9,011)	(19,115)
Other income (expense), net:		
Interest expense, net	(1,188)	(611)
Change in fair value of PIPE Warrant liability	—	(2,396)
	(1,188)	(3,007)
Net loss	$ (10,199)	$ (22,122)
Basic and diluted net loss per share		
Net loss per share	$ (0.30)	$ (0.81)
Weighted average number of common shares outstanding	34,475	27,429

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

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

	Three Months Ended March 31,	
	2022	**2021**
Net loss	$ (10,199)	$ (22,122)
Other comprehensive loss:		
Unrealized gain on available-for-sale securities	4	—
Comprehensive loss	$ (10,195)	$ (22,122)

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, 2021	34,475	$ 34	$ 720,386	$ (3)	$ (674,547)	$ 45,870
Stock-based compensation expense related to equity-classified awards	—	—	1,267	—	—	1,267
Unrealized gain on available-for-sale investments	—	—	—	4	—	4
Net loss	—	—	—	—	(10,199)	(10,199)
Balance at March 31, 2022	34,475	$ 34	$ 721,653	$ 1	$ (684,746)	$ 36,942

See accompanying notes.

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 Cash Flows
(In thousands)
(Unaudited)

	For the Three Months Ended March 31,	
	2022	**2021**
Operating activities		
Net loss	$ (10,199)	$ (22,122)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	17	17
Stock-based compensation	1,267	1,204
Non-cash interest expense	230	140
Non-cash change in fair value of PIPE Warrant liability	—	2,396
Amortization of premium and discount on investments	72	—
Changes in operating assets and liabilities:		
Trade receivables, net	(3,132)	(1,144)
Partnership receivables	959	(225)
Inventory	(38)	—
Prepaid expenses and other current assets	933	468
Operating lease right-of-use asset	99	113
Other non-current assets	—	(100)
Accounts payable	302	583
Accrued clinical trial costs and contract research	1,726	735
Accrued compensation and benefits	(1,494)	(1,414)
Other accrued liabilities	1,620	1,674
Operating lease liability	(3)	(38)
Deferred revenue	(578)	(493)
Deferred research and development reimbursements	—	(52)
Operating lease liability, non-current	—	(76)
Net cash used in operating activities	(8,219)	(18,334)
Investing activities		
Purchases of marketable securities	(2,992)	—
Proceeds from maturities and sales of marketable securities	14,515	—
Net cash provided by investing activities	11,523	—
Financing activities		
Proceeds from issuance of common stock, net of issuance costs	—	54,980
Proceeds from warrant exercises	—	3,092
Proceeds from issuance of loan payable	—	20,000
Payment of debt issuance costs	—	(85)
Net cash provided by financing activities	—	77,987
Net increase in cash and cash equivalents	3,304	59,653
Cash and cash equivalents at beginning of period	70,542	61,761
Cash and cash equivalents at end of period	$ 73,846	$ 121,414
Supplemental cash flow information		
Cash paid for interest	$ 937	$ 362

See accompanying notes.

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is a commercial stage, oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. The Company currently markets FOTIVDA® (tivozanib) in the United States. FOTIVDA is the Company's first commercial 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 for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma ("RCC") following two or more prior systemic therapies. The Company continues to develop tivozanib in immuno-oncology combinations in RCC and other indications, and the Company has other investigational programs in clinical development.

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 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 and is available to patients through a network of specialty pharmacies and distributors. The Company markets and sells FOTIVDA in the United States through its commercial infrastructure.

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, the Company and its collaboration partners are continuing to develop tivozanib in RCC and in additional cancer indications with significant unmet medical needs including, hepatocellular carcinoma ("HCC"), and tumors that are resistant to immunotherapy, or immunologically cold tumors, in combination with immune checkpoint inhibitors ("ICIs"). In addition, the Company is evaluating tivozanib as a monotherapy in ovarian cancer and cholangiocarcinoma ("CCA"). The Company and the Company's collaboration partners or independent investigators sponsor the development of tivozanib through preclinical studies and clinical trials conducted under collaboration agreements and investigator sponsored trial ("IST") agreements or the Company's Cooperative Research and Development Agreement ("CRADA") with the National Cancer Institute's Surgical Oncology Program ("NCI-SOP").

The Company is also seeking to advance its pipeline of four wholly owned immunoglobulin G1 ("IgG1") monoclonal antibody product candidates, ficlatuzumab, AV-380, AV-203 and AV-353. The Company aims to leverage its existing collaborations and partnerships and enter into new strategic collaborations and partnerships to continue to advance each of its product candidates.

As used throughout these 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, 2022, the Company has financed its operations primarily through private placements and public offerings of its common stock, license fees, milestone payments and research and development funding from strategic partners, FOTIVDA commercial sales receipts and debt facilities. 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, commercializing FOTIVDA, 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 portfolio 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 payors 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 $684.7 million as of March 31, 2022. 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 and preclinical stage assets. The Company may require substantial additional capital to continue to advance its pipeline of clinical and preclinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources, principally product sales of FOTIVDA in the United States.

As of May 5, 2022, the date of issuance of these consolidated financial statements, the Company expects that its cash, cash equivalents and marketable securities of $79.0 million as of March 31, 2022, along with net product revenues from product sales 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 capital 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 the commercialization of its product.

(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, 2022 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2022 or any other future period.

The information presented in the condensed consolidated financial statements and related footnotes at March 31, 2022, and for the three months ended March 31, 2022 and 2021, is unaudited, and the condensed consolidated balance sheet amounts and related footnotes as of December 31, 2021 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, 2021, which was filed with the U.S. Securities and Exchange Commission ("SEC") on March 14, 2022.

(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 (collectively with the specialty pharmacies, the "Customers" and each a "Customer"). 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 trade receivables (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 over time 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 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, Medicare Part D Coverage Gap Discounts 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. In addition, 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 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 over time as FOTIVDA is the Company's first commercial product. Rebates are generally invoiced by the payor 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 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.

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 in the United States earned in the three months ended March 31, 2022 and 2021, respectively (in thousands):

	Three Months Ended March 31,	
	2022	2021
Product revenues:		
Gross product revenues	$ 24,644	$ 1,256
Discounts and allowances	(4,558)	(190)
Net product revenues	$ 20,086	$ 1,066

The following table summarizes the percentage of total product revenues for FOTIVDA in the United States by any Customer who individually accounted for 10% or more of total product revenues earned in the three months ended March 31, 2022 and 2021, respectively:

	Three Months Ended March 31,	
	2022	2021
Affiliates of McKesson Corporation	42 %	33 %
Affiliates of AmerisourceBergen Corporation	28 %	23 %
OncoMed Specialty, LLC (Onco360)	23 %	31 %
Affiliates of Cardinal Health Specialty	7 %	13 %
	100 %	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, 2022 were as follows (in thousands):

	Chargebacks, Discounts for Prompt Pay and Other Allowances	Rebates, Customer Fees / Credits and Co-Pay Assistance	Totals
Balance at December 31, 2021	$ 1,193	$ 1,170	$ 2,363
Provision related to sales made in:			
Current period	2,598	1,960	4,558
Prior periods	—	—	—
Payments and customer credits issued	(2,402)	(943)	(3,345)
Balance at March 31, 2022	$ 1,389	$ 2,187	$ 3,576

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 other current accrued liabilities 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 are determined at contract inception and are not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining SSP for performance obligations requires significant judgment. In developing 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 SSP for performance obligations by evaluating whether changes in the key assumptions used to determine 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, 2022 and 2021, respectively, by partner (in thousands). Refer to Note 4, *"Collaborations and License Agreements"* regarding specific details.

	Three Months Ended March 31,	
	2022	2021
EUSA	$ 834	$ 854
Total	$ 834	$ 854

Trade Receivables

Trade receivables, net, includes amounts billed to 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 considers its historical losses, if any, adjusted to account for current conditions, and reasonable and supportable forecasts of future economic conditions affecting its customers to estimate credit losses. The 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 the Company's 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 considered regulatory approval of its product candidate to be uncertain and product manufactured prior to regulatory approval could not have been sold unless regulatory approval was 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. In 2021, the Company conducted resupply manufacturing of tivozanib in connection with upcoming drug expirations beginning in the fourth quarter of 2022. As of March 31, 2022, the Company capitalized approximately $1.7 million of manufacturing costs as Inventory on the Consolidated Balance Sheet, all of which was classified as work in process.

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.

Cash and Cash Equivalents

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 did not have any restricted cash balances at March 31, 2022.

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, 2022 and December 31, 2021 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
March 31, 2022				
Cash and cash equivalents:				
Cash and money market funds	$ 73,846	$ —	$ —	$ 73,846
Total cash and cash equivalents	73,846	—	—	73,846
Marketable securities:				
Government agency securities due within 1 year	$ 2,991	$ 1	$ —	$ 2,992
Corporate debt securities due within 1 year	$ 2,200	$ —	$ —	$ 2,200
Total marketable securities	5,191	1	—	5,192
Total cash, cash equivalents and marketable securities	**$ 79,037**	**$ 1**	**$ —**	**$ 79,038**
December 31, 2021				
Cash and cash equivalents:				
Cash and money market funds	$ 70,542	$ —	$ —	$ 70,542
Total cash and cash equivalents	70,542	—	—	70,542
Marketable securities:				
Corporate debt securities due within 1 year	$ 16,787	$ —	$ (3)	$ 16,784
Total marketable securities	16,787	—	(3)	16,784
Total cash, cash equivalents and marketable securities	**$ 87,329**	**$ —**	**$ (3)**	**$ 87,326**

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 Customers for product sales of FOTIVDA. The 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, 2022, 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 and had financial assets based on Level 2 inputs consisting of high-grade debt securities, including commercial paper. During the three months ended March 31, 2022, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of March 31, 2022, the Company did not have any financial liabilities recorded at fair value.

The loan payable (discussed in Note 6), which is classified as a Level 3 liability, has a variable interest rate and the carrying value approximates its fair value. As of March 31, 2022, the carrying value was approximately $38.2 million.

The following table summarizes the financial assets and liabilities measured at fair value on a recurring basis at March 31, 2022 and December 31, 2021 (in thousands):

	Fair Value Measurements as of March 31, 2022			
	Level 1	Level 2	Level 3	Total
Financial assets carried at fair value:				
Cash and money market funds	$ 73,846	$ —	$ —	$ 73,846
Total cash and cash equivalents	$ 73,846	$ —	$ —	$ 73,846
Marketable securities:				
Government agency securities due within 1 year	$ —	$ 2,992	$ —	$ 2,992
Corporate debt securities due within 1 year	$ —	$ 2,200	$ —	$ 2,200
Total marketable securities	$ —	$ 5,192	$ —	$ 5,192
Total cash, cash equivalents and marketable securities	**$ 73,846**	**$ 5,192**	**$ —**	**$ 79,038**

	Fair Value Measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Financial assets carried at fair value:				
Cash and money market funds	$ 70,542	$ —	$ —	$ 70,542
Total cash and cash equivalents	$ 70,542	$ —	$ —	$ 70,542
Marketable securities:				
Corporate debt securities due within 1 year	$ —	$ 16,784	$ —	$ 16,784
Total marketable securities	$ —	$ 16,784	$ —	$ 16,784
Total cash, cash equivalents and marketable securities	**$ 70,542**	**$ 16,784**	**$ —**	**$ 87,326**

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, 2022 and 2021, 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 until the expirations of the Offering Warrants on April 8, 2021 and the PIPE Warrants on May 16, 2021 would be anti-dilutive.

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, 2022 and 2021, respectively (in thousands):

	Outstanding at March 31,	
	2022	2021
Stock options outstanding	5,266	3,068
Offering Warrants outstanding (warrants expired April 8, 2021)	—	2,253
PIPE Warrants outstanding (warrants expired May 16, 2021)	—	1,684
Total	5,266	7,005

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 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, 2022 and 2021, the Company recorded the following stock-based compensation expense (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development	$ 212	$ 355
Selling, general and administrative	1,055	849
Total	$ 1,267	$ 1,204

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, 2022, the Company is forecasting an effective tax rate of 0% for the year ending December 31, 2022. 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, 2022 and 2021, the Company had 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 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, 2022 and 2021, 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, 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.

(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 to evaluate the safety and efficacy of AstraZeneca's IMFINZI (durvalumab), a human monoclonal antibody directed against PD-L1, in combination with tivozanib as a first-line treatment or following bevacizumab and atezolizumab 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 in each of the three months ended March 31, 2022 and 2021, respectively. The amount due to the Company from AstraZeneca pursuant to the cost-sharing provision was approximately $0.5 million as of March 31, 2022.

Out-License Agreements

EUSA

In December 2015, the Company entered into a license agreement with EUSA (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. In March of 2022, EUSA was acquired by Recordati, S.p.A ("Recordati"). As a result of the acquisition, all rights and obligations under the EUSA Agreement are transferred to Recordati.

EUSA has made research and development reimbursement and milestone payments to the Company totaling $12.5 million, including (i) a $2.5 million upfront payment upon the execution of the EUSA Agreement in December 2015, (ii) a $4.0 million research and development payment in September 2017 upon its receipt of marketing approval from the European Commission in August 2017 for FOTIVDA (tivozanib) for the treatment of RCC, and (iii) three $2.0 million milestones upon its receipt of reimbursement approvals in each of (a) February 2018 from the National Institute for Health and Care Excellence ("NICE") in the United Kingdom, (b) November 2018 from the German Federal Association of the Statutory Health Insurances ("GKV-SV") in Germany and (c) February 2019 from the Ministry of Health, Consumer Affairs and Social Welfare ("MSCBS") in Spain These reimbursement milestones payments were received in March 2018, December 2018 and May 2019, respectively. In addition, in September 2017, EUSA elected to opt-in to co-develop the Phase 2 clinical trial of tivozanib in combination with nivolumab in the first-line and the second-line treatment of RCC (the "TiNivo trial"). EUSA made an additional research and development reimbursement payment to the Company of $2.0 million in October 2017, in advance of the completion of the TiNivo trial for its approximate 50% share of the total costs of the TiNivo trial.

As of March 31, 2022, the Company is eligible to receive (i) a $2.0 million milestone payment with respect to reimbursement approval in each of France and Italy, (ii) an additional $2.0 million for the grant of marketing approval for RCC in the three licensed countries outside of the EU, as mutually agreed by the parties, of which two approvals have been obtained in New Zealand in July 2019 and in South Africa in September 2020, (iii) a payment of $2.0 million per indication in connection with a filing by EUSA with the European Medicines Agency ("EMA") for marketing approval for tivozanib for the treatment of each of up to three additional indications, (iv) $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, and (v) up to $335.0 million upon EUSA's achievement of certain sales thresholds. In addition, 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 any research and development reimbursement payments were earned in the three months ended March 31, 2022 and 2021. The Company is also eligible to receive an additional research and development reimbursement payment of up to $20.0 million, for the Company's Phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, sorafenib (Nexavar®), in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies (the "TIVO-3 trial"), if Recordati elects to opt-in to that study.

Pursuant to the KKC Agreement (as defined below), the Company is required to pay KKC a 30% sublicense fee related to earned milestone payments and royalties from EUSA. However, research and development reimbursement payments by EUSA are excluded from the 30% sublicense fee due to KKC, subject to certain limitations. If Recordati elects to opt-in to the TIVO-3 trial, only approximately $8.7 million of the $20.0 million research and development payment would be subject to the 30% sublicense fee due to KKC. 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 sub-license fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

Recordati, following its acquisition of EUSA, is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout the EUSA Licensed Territories in RCC. Recordati 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 $12.5 million aggregate transaction price, as described above, were being recognized as collaboration and licensing revenue over the Company's estimated substantive performance period. Under ASC 606, upon the achievement of a regulatory milestone, the amount that represented the cumulative catch-up for the period from contract execution in December 2015 through the date of the milestone achievement was 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. As of March 31, 2022, the Company has determined that it has fulfilled its performance obligations under the contract in accordance with ASC 606 as the license was previously transferred and the Company is not currently providing substantive support under the EUSA Agreement. The Company recognized license and collaboration revenue of approximately $0.6 million and $0.5 million in the three months ended March 31, 2022 and 2021, respectively.

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. The Company will assess any substantive performance obligations in connection with the achievement of future regulatory-related milestones. If the Company does not have any substantive performance obligations, the full amount of the milestone will be recognized in the period the milestone is achieved.

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 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 EUSA licensed territories. The Company recognized royalty revenue of approximately $0.2 million and $0.4 million in the three months ended March 31, 2022 and 2021, respectively.

The Company recognized total revenues under the EUSA Agreement of approximately $0.8 million and $0.9 million in the three months ended March 31, 2022 and 2021, respectively. The amount due to the Company from EUSA pursuant to the EUSA Agreement was approximately $0.2 million as of March 31, 2022.

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.

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 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 excluding contributions to research and development expenses 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.

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 is 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-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 AG 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, 2022, the Company is required to make future milestone payments, up to an aggregate total of $12.1 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. In February 2022, the Company paid a $2.3 million time-based milestone obligation which became due to St. Vincent's in January 2022. 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.

The St. Vincent's Agreement remains in effect until the later of ten years after the date of first commercial sale of licensed therapeutic products in the last country in which a commercial sale is made, or expiration of the last-to-expire valid claim of the licensed patents, unless we elect, or St. Vincent's elects, to terminate the St. Vincent's Agreement earlier. We have the right to terminate the St. Vincent's Agreement on six months' notice if we terminate our GDF15 research and development programs as a result of the failure of a licensed therapeutic product in preclinical or clinical development, or if we form the reasonable view that further GDF15 research and development for the treatment of cachexia is not commercially viable, and we are not then in breach of any of our obligations under the St. Vincent's Agreement.

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 made a non-refundable upfront payment to the Company in the amount of $25.0 million that was received in September 2019, and KKC waived the one-time milestone payment of $18.0 million which would have otherwise been payable by the Company upon obtaining marketing approval on March 10, 2021 for tivozanib in the United States. KKC is 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.

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 clinical trial of tivozanib for the first-line treatment of RCC, which we refer to as our 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 New Drug Application filing for tivozanib. Pursuant to the amendment to the KKC Agreement, KKC waived the one-time milestone payment of $18.0 million which would have otherwise been payable by the Company upon obtaining marketing approval on March 10, 2021 for tivozanib in the United States. Each milestone under the KKC Agreement was a one-time only payment obligation.

The Company has no remaining development and commercialization milestone payments due to KKC under the KKC Agreement.

The Company is 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 twelve 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 following two or more prior systemic therapies. On March 22, 2021, the Company commenced product sales of FOTIVDA in the United States. In the three months ended March 31, 2022 and 2021, the Company recognized approximately $2.4 million and $0.1 million, respectively, in royalties due to KKC on net product sales of FOTIVDA in the United States in its Statement of Operations as a component of cost of products sold.

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 for research and development reimbursement payments or equity investments, subject to certain limitations.

In connection with the EUSA Agreement, the Company is required to pay KKC the 30% sublicense fee related to earned milestone payments and royalties from EUSA. However, research and development reimbursement payments by EUSA are excluded from the 30% sublicense fee, subject to certain limitations. If Recordati elects to opt-in to the TIVO-3 trial, only approximately $8.7 million of the $20.0 million research and development payment would be subject to the 30% sublicense fee due to KKC. Refer to the section above, "Out License Agreements – *EUSA"*, for further discussion of the actual 30% sublicense fees incurred and paid to-date to KKC.

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 United States approval of tivozanib, the Company earned and received a $2.8 million development milestone payment in August 2020 pursuant to the amendment to the KKC Agreement upon the acceptance of KKC's investigational new drug, or IND, application for a non-oncology use of tivozanib by the Pharmaceuticals and Medical Devices Agency of Japan on August 2, 2020. KKC is also required to make remaining milestone payments to the Company of up to an aggregate of $387.9 million upon the successful achievement of certain development and sales milestones of tivozanib in non-oncology indications. 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, 2022 and 2021.

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, 2022	December 31, 2021
FOTIVDA U.S. Product Royalties	2,420	2,011
FOTIVDA Federal Rebates, Customer Credits and Co-Pay Assistance	2,187	1,170
Professional Fees	1,497	1,107
Other	937	1,133
Total	7,041	5,421

(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" and as amended by the 2020 Loan Amendment (as defined below), the 2021 Loan Amendment (as defined below) and the 2022 Loan Amendment (as defined below) the "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 is 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 in the initial amount of $10.0 million ("Tranche Two") was available through June 30, 2021 upon achieving FDA approval of FOTIVDA ("Performance Milestone I"), (ii) the third tranche of $5.0 million ("Tranche Three") was initially available from July 1, 2021 through January 31, 2022 assuming the Company was to achieve $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 ("Tranche Four") was initially 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 achieves 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 were scheduled to commence on October 1, 2021 at the earliest, as described above. The interest rate as of March 31, 2022 was 9.90%, based upon an increase in the prime rate in March 2022.

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 continued to be due and was paid 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 was also required to achieve greater than or equal to 75% of its forecasted net product revenues from its sales of tivozanib over a six month trailing period, as defined and measured on a monthly basis, effective upon the earlier of receiving Third Tranche funding and the month of April 2022.

On February 1, 2021, the Company entered into the second amendment to the 2017 Loan Agreement (the “2021 Loan Amendment”), which increased 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 then 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.

On December 22, 2021, the Company completed the $5.0 million drawdown of Tranche Three funding under the 2021 Loan Amendment that was made available in connection with the achievement of Performance Milestone II upon the achievement of $35.0 million in net product revenues from sales of FOTIVDA. The achievement of Performance Milestone II extended the interest-only period by six months from September 30, 2022 to March 31, 2023, extended the loan maturity by one year from September 1, 2023 to September 1, 2024 and decreased the amount of unrestricted cash required for the Company to satisfy the minimum financial covenant from $15.0 million to $10.0 million thereafter through the maturity of the Loan Agreement.

On March 8, 2022, the Company entered into the third amendment to the 2017 Loan Agreement (the "2022 Loan Amendment"). The 2022 Loan Amendment (i) changed the operating covenant to decrease the achievement of greater than or equal to 75% of the Company's forecasted net product revenues from its sales of tivozanib over a six-month trailing period to 65%, as defined and measured on a monthly basis, and extended the month of commencement from April 2022 to June 2022, (ii) added a cash waiver, at the Company's election, in the event its actual net product revenues from its sales of tivozanib over a six-month trailing period are below the monthly minimum operating covenant of 65%, such that the Company's unrestricted cash position is equal to or greater than the then total outstanding principal under the Loan Agreement for each day of such month, (iii) changed Tranche Four funding, in the amount of $5.0 million, that was subject to the consent of Hercules to the achievement of $30.0 million in net product revenues from sales of FOTIVDA over a trailing three-month period, or Performance Milestone III, and extended the availability of Tranche Four funding from June

30, 2022 to December 15, 2022, and (iv) increased the amount of unrestricted cash required for the Company to satisfy the minimum financial covenant from $10.0 million to $15.0 million upon the earlier of receiving the Tranche Four funding or January 1, 2023, through the maturity of the Loan Agreement.

As of March 31, 2022, the total outstanding principal under the Loan Agreement was $40.0 million, principal payments are scheduled to commence on April 1, 2023 and the corresponding end-of-term payments under the Loan Agreement, in the aggregate amount of approximately $2.8 million, are due upon the current loan maturity date of September 1, 2024. As of March 31, 2022, $5.0 million remains available to the Company in committed funding under the Loan Agreement, in Tranche Four funding in connection with the achievement of Performance Milestone III for $30.0 million in net product revenues from sales of FOTIVDA over a trailing three-month period. The unamortized discount to be recognized over the remainder of the loan period was approximately $1.8 million and $2.0 million as of March 31, 2022 and December 31, 2021, respectively. Per the Loan Agreement, the end-of-term payment of approximately $0.8 million was paid on July 1, 2021, as scheduled.

The Loan Agreement is secured by substantially all of the Company's assets, excluding intellectual property. The Loan Agreement provides that certain events shall constitute a default by the Company, including failure by the Company to pay amounts under the Loan Agreement when due; breach or default in the performance of any covenant under the Loan Agreement 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, 2022, 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 Loan Agreement.

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, including interest and principal, under the loans payable outstanding as of March 31, 2022 are as follows (in thousands):

Year Ending December 31:		**Amount**
2022 (remaining nine months)	$	3,021
2023		22,594
2024		24,449
	$	50,064
Less amount representing interest		(7,284)
Less unamortized discount		(1,811)
Less deferred charges		(2,780)
Loans payable, net of discount	$	38,189

(7) Common Stock

As of March 31, 2022, the Company had 50,000,000 authorized shares of common stock, $0.001 par value, of which 34,474,710 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 $51.7 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, 2022, there was approximately $213.0 million available for future issuance of common stock, preferred stock, debt securities, warrants and/or units.

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, 2022, approximately $22.2 million was available for issuance in connection with future stock sales pursuant to the SVB Leerink Sales Agreement.

(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. This amendment was approved by stockholders at the Annual Meeting of Stockholders held on June 10, 2020. In April 2021, the board of directors adopted an additional amendment to the 2019 Plan to increase the total number of shares reserved under the Plan by 2,200,000. This amendment was approved by stockholders at the Annual Meeting of Stockholders held on June 9, 2021.

Awards may be made under the 2019 Plan for up to the sum of (i) 4,500,000 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, 2022, there were 288,181 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, 2022:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2022	3,156,379	$ 9.45	7.55	$ 5,720
Granted	2,122,976	3.68		
Exercised	—	—		
Forfeited	(10,043)	48.15		
Outstanding at March 31, 2022	5,269,312	$ 7.05	8.30	$ 4,131,736
Exercisable at March 31, 2022	1,608,347	$ 10.84	6.03	$ 111,672

The aggregate intrinsic value is based upon the Company's closing stock price of $5.59 on March 31, 2022.

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. The following tables summarize the assumptions used in the Black-Scholes option-pricing model in the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,	
	2022	2021
Volatility factor	97.19% - 97.79%	56.17% - 102.66%
Expected term (in years)	6.25	0.25 - 6.25
Risk-free interest rates	1.69% - 2.20%	0.06% - 1.13%
Dividend yield	—	—

Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the three months ended March 31, 2022 and 2021 was $2.91 and $7.03, respectively.

As of March 31, 2022, there was $15.0 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 3.32 years.

Employee Stock Purchase Plan

In February 2010, the board of directors adopted the 2010 Employee Stock Purchase Plan (the "ESPP"), as amended in March 2013 and in November 2017. In April 2021, the board of directors adopted an amendment to the 2010 ESPP Plan to increase the total number of shares reserved under the Plan by 500,000 shares, pursuant to which the Company may sell up to an aggregate of 576,400 shares of Common Stock. This amendment was approved by stockholders at the Annual Meeting of Stockholders held on June 9, 2021. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each six-month period during the term of the ESPP. As of March 31, 2022, there were 412,403 shares available for future issuance under the ESPP.

The Company did not sell any shares of common stock pursuant to the ESPP during the three months ended March 31, 2022 and March 31, 2021. The total stock-based compensation expense recorded as a result of the ESPP was $0.1 million during the three months ended March 31, 2022 and March 31, 2021, respectively.

(13) Legal Proceedings

As of the date of filing this Quarterly Report on Form 10-Q, there are no material 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 consolidated financial statements and the related notes appearing elsewhere in this report. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section in Part II, Item 1A of this report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a commercial stage, oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. We currently market FOTIVDA® (tivozanib) in the United States. FOTIVDA is our first commercial 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 for the treatment of adult patients with relapsed or refractory advanced, or R/R, renal cell carcinoma, or RCC, following two or more prior systemic therapies. We continue to develop tivozanib in immuno-oncology combinations in RCC and other indications, and we have other investigational programs in clinical development.

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 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 and is available to patients through a network of specialty pharmacies and distributors. We market and sell FOTIVDA in the United States through our commercial infrastructure. Based on third party data, we believe we took a leadership position in the number of new third-line R/R RCC patient starts during the first quarter of 2022, suggesting that FOTIVDA was being more broadly adopted in the third-line R/R RCC setting. We believe this is a leading indicator of progress toward our objective to become the market share leader and the standard of care in the third-line R/R RCC setting.

Restrictions related to the ongoing COVID-19 pandemic have posed challenges for gaining in-person access to customers, prescribers and other healthcare professionals and certain institutions remain closed to industry representatives. Notwithstanding these challenges, as of March 31, 2022, prescriptions for FOTIVDA and product revenues have increased quarter over quarter since the beginning of our commercial launch. We aim to continue to deliver quarter over quarter net revenue and underlying prescription demand growth as we continue to execute on our commercial strategy to support the adoption of FOTIVDA in appropriate patients.

We believe there is significant commercial opportunity for FOTIVDA in RCC in the United States. Based on third party estimates, the current U.S. market for R/R RCC therapy is more than $1.7 billion, including $1.3 billion in the second line and $480.0 million in the third and fourth lines. Data from the TIVO-3 trial demonstrated the superior efficacy and improved tolerability of FOTIVDA when compared to an approved VEGFR TKI in the RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies, and we believe that FOTIVDA could become a standard of care in the United States in the third line relapsed or refractory advanced setting. Further, we are seeking to generate data to support regulatory approval of tivozanib in combination with nivolumab in the second line R/R RCC setting, which represents a larger market opportunity than the third line R/R RCC setting, through our Phase 3 clinical trial designed to evaluate the safety and efficacy of tivozanib in combination with nivolumab as compared to tivozanib monotherapy in RCC patients who have progressed following one or two lines of therapy, one of which was an immune checkpoint inhibitor, or ICI, which we refer to as the TiNivo-2 trial. We and our collaboration partners are also developing tivozanib in combination with ICIs and a hypoxia inducible factor 2α, or HIF2α, inhibitor to support the expansion of tivozanib's potential utility in RCC.

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, we and our collaboration partners are continuing to develop tivozanib in RCC and in additional cancer indications with significant unmet medical needs including hepatocellular carcinoma, or HCC, and tumors that are resistant to immunotherapy, or immunologically cold tumors, in combination with ICIs. In addition, we are evaluating tivozanib as a monotherapy in ovarian cancer and cholangiocarcinoma, or CCA. We and our collaboration partners or independent investigators sponsor the development of tivozanib through preclinical studies and clinical trials conducted under

collaboration agreements and investigator sponsored trial, or IST, agreements or our Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute's Surgical Oncology Program, or NCI-SOP.

We are also seeking to advance our pipeline of four wholly owned IgG1, monoclonal antibody product candidates, ficlatuzumab, AV-380, AV-203 and AV-353. We aim to leverage our existing collaborations and partnerships and enter into new strategic collaborations and partnerships to continue to advance each of our product candidates.

Business Update Regarding COVID-19

The COVID-19 pandemic has and will continue to affect economies and businesses around the world. We continue to closely monitor the impact of the COVID-19 pandemic on all aspects of our business, including the impact on our employees, patients, communities and business operations to varying degrees. We have and may continue to experience disruptions in the future that could directly or indirectly impact our results of operations, including product revenue and our financial condition. Although we do not currently expect that the ongoing COVID-19 pandemic will have a material impact on our business plans or results of operations, we are unable to predict the impact that the COVID-19 pandemic will have on our operating results and financial condition due to numerous uncertainties. These uncertainties include the duration, scope and severity of the pandemic, the duration and extent of travel restrictions and social distancing in the United States and other countries, business closures and business disruptions, its impact and the economic impact on local, regional, national and international markets, the effectiveness of actions taken in the United States and other countries to contain and treat the disease, periodic and seasonal spikes in infection rates, new strains of the virus that cause outbreaks of COVID-19 and the broad availability of effective vaccines and antiviral treatments, among others. The situation surrounding the COVID-19 pandemic remains fluid and continues to rapidly evolve, and we are actively managing our response and assessing potential impacts to our operating results and financial condition, as well as adverse developments in our business. For further information regarding the impact of the COVID-19 pandemic on us, see Item 1A - Risk Factors included 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, 2022, we had an accumulated deficit of $684.7 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 and preclinical stage assets.

We may require substantial additional capital to continue to advance our pipeline of clinical and preclinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources, principally product sales of FOTIVDA in the United States. Please 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" of this Quarterly Report for a further discussion of our funding requirements.

Revenue

Prior to the commercial launch of FOTIVDA in March 2021, our revenues were historically 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.

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 collaboration 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 is net of amounts reimbursed under our clinical supply agreement with a wholly owned subsidiary of AstraZeneca for their respective share of development costs incurred by us in connection with our open-label, multi-center, randomized Phase 1b/2 clinical trial to evaluate the safety and efficacy of AstraZeneca's IMFINZI (durvalumab), a human monoclonal antibody directed against PD-L1, in combination with tivozanib as a first-line treatment or following bevacizumab and atezolizumab treatment for patients with advanced, unresectable HCC, which we refer to as our DEDUCTIVE trial.

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.

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, 2022, we are forecasting an effective tax-rate of 0% for the year ending December 31, 2022, 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 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 and critical accounting estimates are described in the notes to our consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Results of Operations

Comparison of three months ended March 31, 2022 and 2021

Revenues (in thousands)

	Three Months Ended March 31,		Change	
	2022	2021	$	%
FOTIVDA U.S. product revenue, net	$ 20,086	$ 1,066	$ 19,020	1,784 %
Partnership revenue - EUSA	834	854	(20)	(2)%
Total revenues	$ 20,920	$ 1,920	$ 19,000	990 %

Our total revenues increased by $19.0 million, or 990%, to $20.9 million in the three months ended March 31, 2022 from $1.9 million in the same period in 2021, principally due to the commencement of sales of our first commercial 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.

FOTIVDA U. S. Product Revenue, Net (in thousands)

	Three Months Ended March 31,		Change	
	2022	2021	$	%
Gross product revenue	$ 24,644	$ 1,256	$ 23,388	1,862 %
Discounts and allowances	(4,558)	(190)	(4,368)	2,299 %
Product revenue, net	$ 20,086	$ 1,066	$ 19,020	1,784 %

We commenced sales of our first commercial 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.

We anticipate FOTIVDA net product revenues will be in the range of $100.0 million to $110.0 million in 2022.

Cost of Products Sold (in thousands)

	Three Months Ended March 31,		Change	
	2022	2021	$	%
Cost of products sold	$ 2,434	$ 138	$ 2,296	1,664 %
Gross margin %	88 %	87 %		

We commenced sales of our first commercial 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 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 continue to be in the mid-to-high 80th percentile in 2022.

Research and Development Expenses (in thousands)

	Three Months Ended March 31,		Change	
	2022	2021	$	%
Tivozanib	$ 3,843	$ 3,856	$ (14)	— %
AV-380 Program in Cachexia	2,889	766	2,124	277 %
Ficlatuzumab	2,933	450	2,483	552 %
Overhead	496	725	(229)	(32 %)
Total research and development expenses	$ 10,160	$ 5,797	$ 4,363	75 %

Our total research and development expenses increased by $4.4 million, or 75%, to $10.2 million in the three months ended March 31, 2022 from $5.8 million in the same period in 2021.

Tivozanib expenses decreased in the three months ended March 31, 2022 as compared to the same period in 2021, principally related to costs incurred in the first quarter of 2021 for the TIVO-3 trial that were not incurred in the same period in 2022 as the trial was closed in the second half of 2021 following FDA approval of FOTIVDA on March 10, 2021, offset by an increase in costs incurred in connection with the TiNivo-2 trial that was initiated in the first quarter of 2021.

AV-380 expenses increased by $2.1 million, or 277%, in the three months ended March 31, 2022 as compared to the same period in 2021, principally related to a $2.3 million time-based milestone obligation that became due to St. Vincent's in January 2022.

Ficlatuzumab expenses increased by $2.5 million, or 552%, in the three months ended March 31, 2022 as compared to the same period in 2021, principally related to the $2.4 million increase in costs incurred in connection with the conduct of certain manufacturing activities in support of planned clinical drug supply manufacturing in 2022 for a potential registrational clinical trial of ficlatuzumab in combination with cetuximab in patients with human papillomavirus, or HPV, negative recurrent or metastatic, or R/M, head and neck squamous cell carcinoma, or HNSCC patients in the first half of 2023.

We anticipate that research and development expenses will increase in 2022, principally related to the enrollment of the TiNivo-2 Trial for the treatment of RCC patients who have progressed following one or two lines of therapy, one of which was an ICI, the manufacturing of ficlatuzumab clinical drug supply for a potential registrational clinical trial in HPV negative R/M HNSCC patients that we plan to initiate in the first half of 2023, a Phase 1b clinical trial in AV-380 in cancer patients that we plan to initiate in the second half of 2022 and the related manufacturing of AV-380 clinical drug supply, and co-funding pursuant to the clinical trial collaboration and supply agreement with NiKang Therapeutics Inc. for a Phase 2 clinical trial to evaluate tivozanib in combination with NKT2152 in clear cell RCC patients who have not responded to or relapsed from prior therapies. These increases in 2022 research and development expenses will be partially offset by lower costs, principally related to the TIVO-3 Trial that closed in the second half of 2021 following the FDA's approval of FOTIVDA on March 10, 2021. We anticipate that research and development expenses will be in the range of $60.0 million to $70.0 million in 2022 in support of our existing pipeline plans. The timing and nature of contemplated activities in 2022 will be conducted subject to the availability of sufficient financial resources.

Selling, General and Administrative Expenses (in thousands)

	Three Months Ended March 31,		Change	
	2022	2021	$	%
Selling, general and administrative expenses	$ 17,337	$ 15,100	$2,237	15 %

Selling, general and administrative expenses increased by $2.2 million, or 15%, to $17.3 million in the year ended March 31, 2022 from $15.1 million in the same period in 2021. The $2.2 million increase was principally due to increases totaling $2.6 million, including: (i) $1.4 million in connection with compensation costs related to a full quarter of growth in our commercial infrastructure, including the hiring of our salesforce in the first quarter of 2021, (ii) $0.7 million in connection with external commercial activities in marketing, market access and commercial operations for a full quarter of commercialization following the launch of FOTIVDA on March 22, 2021, and (iii) $0.5 million in general and

administrative-related compensation costs. These increases were partially offset by a $0.4 million decrease in general and administrative-related professional fees.

We anticipate that selling, general and administrative expenses associated with the commercialization of FOTIVDA, principally related to our sales force, our marketing, market access and commercial capabilities, and general and administrative support will increase in 2022, principally reflective of a full year of commercialization following the launch of FOTIVDA on March 22, 2021.We anticipate that selling, general and administrative expenses will be approximately $70.0 million, including approximately $50.0 million in commercial expenses and approximately $20.0 million in general and administrative expenses.

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

	Three Months Ended March 31,		Change	
	2022	2021	$	%
Change in fair value of expired PIPE Warrant liability	$ —	(2,396)	$ 2,396	(100 %)

In May 2016, we issued warrants in connection with a private placement financing, or the PIPE Warrants, and recorded the warrants as a liability. The PIPE Warrants were exercisable for a period of five years from the date of issuance until their scheduled expiration on May 16, 2021. The PIPE Warrants were subject to revaluation at each balance sheet date and any changes in fair value were 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. The PIPE Warrants expired in their entirety on May 16, 2021.

Interest Expense, net (in thousands)

	Three Months Ended March 31,		Change	
	2022	2021	$	%
Interest expense, net	$ (1,188)	$ (611)	$ (577)	94 %

Interest expense, net increased by $0.6 million, or 94%, in the three months ended March 31, 2022, as compared to the same period in 2021, principally due to higher loan balances under the 2020 Loan Amendment and 2021 Loan Amendment, as defined below, that were entered into with Hercules Capital Inc. and certain of its affiliates, or Hercules, on August 7, 2020 and February 1, 2021. respectively. 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 and 2021 Loan Amendment.

We anticipate that interest expense, net will increase in 2022 due to the $40.0 million loan balance as of March 31, 2022, the extended interest-only period through March 2023 pursuant to the 2020 Loan Amendment and 2021 Loan Amendment with Hercules, and the increase in the interest rate in March 2022 from 9.65% to 9.90%.

Liquidity and Capital Resources

We have financed our operations to date primarily through private placements and public offerings of our common stock, license fees, milestone, royalty payments and research and development funding from strategic partners, loan proceeds and sales revenues of our first commercial product FOTIVDA in the United States. As of March 31, 2022 we had cash, cash equivalents and marketable securities of approximately $79.0 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.

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

	For the Three Months Ended March 31,	
	2022	2021
Net cash used in operating activities	$ (8,219)	$ (18,334)
Net cash provided by investing activities	11,523	—
Net cash provided by financing activities	—	77,987
Net increase in cash and cash equivalents	$ 3,304	$ 59,653

Our operating activities used cash of $8.2 million and $18.3 million in the three months ended March 31, 2022 and 2021, 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 $11.5 million in the three months ended March 31, 2022, principally due to net change in the purchases and maturities of marketable securities. We did not have any marketable securities in the three months ended March 31, 2021.

Our financing activities provided cash of $78.0 million in the three months ended 2021. 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 in March 2021 related to the achievement of the milestone for FDA approval of FOTIVDA, 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..

We did not raise any proceeds from equity financings or draw down any loan funding pursuant to the Hercules Loan Facility in the three months ended March 31, 2022.

Hercules Loan Facility ($45 Million Loan Facility - $5 Million Committed Funding Remaining)

On May 28, 2010, we 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.

We entered into the first amendment to the 2017 Loan Agreement, or the 2020 Loan Amendment, on August 7, 2020, the second amendment to the 2017 Loan Agreement, or the 2021 Loan Amendment, on February 1, 2021 and the third amendment to the 2017 Loan Agreement, or the 2022 Loan Amendment, on March 8, 2022, which we collectively refer to as the Loan Agreement to provide a $45.0 million loan facility.

On March 8, 2022, we entered into the 2022 Loan Amendment, which (i) changed the operating covenant to decrease the achievement of greater than or equal to 75% of our forecasted net product revenues from our sales of tivozanib over a six-month trailing period to 65%, as defined and measured on a monthly basis, and extended the month of commencement from April 2022 to June 2022, and (ii) added a cash waiver, at our election, in the event our actual net product revenues from our sales of tivozanib over a six-month trailing period are below the monthly minimum operating covenant of 65%, such that our unrestricted cash position is equal to or greater than the then total outstanding principal under the Loan Agreement for each day of such month, (iii) changed Tranche Four funding, in the amount of $5.0 million, that was subject to the consent of Hercules to the achievement of $30.0 million in net product revenues from sales of FOTIVDA over a trailing three-month period, or Performance Milestone III, and extended the availability of Tranche Four funding from June 30, 2022 to December 15, 2022, and (iv) increased the amount of unrestricted cash required for us to satisfy the minimum financial covenant from $10.0 million to $15.0 million upon the earlier of receiving the Tranche Four funding or January 1, 2023, through the maturity of the Loan Agreement.

As of March 31, 2022, the total outstanding principal under the Loan Agreement was $40.0 million, principal payments are scheduled to commence on April 1, 2023 and the corresponding end-of-term payments under the Loan Agreement, in the aggregate amount of approximately $2.8 million, are due upon the current loan maturity date of September 1, 2024. The interest rate as of March 31, 2022 was 9.90%, based upon an increase in the prime rate in March

2022. As of March 31, 2022, $5.0 million remains available to us in committed funding under the Loan Agreement for Tranche Four funding in connection with the achievement of Performance Milestone III for $30.0 million in net product revenues from sales of FOTIVDA over a trailing three-month period.

Per 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 6.95% of the aggregate amount of loan funding received under the Loan Agreement on the earlier of the maturity of the loan or the date on which we prepay any outstanding loan balance.

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.

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 $0.5 million; 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, 2022, 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 2020 Loan Facility.

See Note 6 to the consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q for a further discussion of our Loan Agreement with Hercules.

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 $51.7 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 $50.0 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, 2022, 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, 2022, there was approximately $213.0 million available for future issuance of our common stock, preferred stock, debt securities, warrants and/or units.

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 and preclinical 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 continue to advance our pipeline of clinical and preclinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources, principally product sales of FOTIVDA in the United States.

During the three months ended March 31, 2022, we received an aggregate of approximately $19.4 million in funding, including approximately $17.8 million in net cash receipts from the product sales of FOTIVDA in the United States and approximately $1.6 million in partnership cost sharing payments.

We believe that our $79.0 million in cash, cash equivalents and marketable securities as of March 31, 2022, along with net product revenues from product sales of FOTIVDA in the United States would enable us to maintain our current operations for more than 12 months following the filing of this Quarterly Report on Form 10-Q.

In 2022, we anticipate FOTIVDA net product revenues will be in the range of $100.0 million to $110.0 million. In 2022, we anticipate that research and development expenses will be in the range of $60.0 million to $70.0 million and selling, general and administrative expenses will be approximately $70.0 million, including approximately $50.0 million in commercial expenses and approximately $20.0 million in general and administrative expenses.

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;
- the impact of COVID-19 on our operations, business and prospects;
- 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 2020 Loan Facility, 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; and
- general economic, industry and market conditions.

We may require substantial additional funding to continue to advance our pipeline of clinical and preclinical 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 milestone specified in the Loan Agreement that would allow us to access the remaining $5.0 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 and preclinical stage assets, whether on terms that are acceptable to us, or at all or if we were to default under the 2020 Loan Facility, 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, preclinical studies 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, 2021 filed with the SEC on March 14, 2022, except as discussed below.

Winter Street Lease

On April 4, 2022, we entered into an office lease agreement (the "Office Lease") to continue leasing our current 6,465 square foot office space at 30 Winter Street in Boston, Massachusetts for an additional two (2) years beginning on November 30, 2022 and ending on November 29, 2024. Under the Office Lease, we will continue to lease the office space for $50.00 per square foot, or approximately $0.3 million in base rent for the first year and $51.00 per square foot, or approximately $0.3 million for the remaining year until the expiration date, each exclusive of operating expenses and taxes.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company, as defined by Rule 12b-2 of the Securities Exchange Act of 1934, as amended, and are not required to provide the information required under this Item 3.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief 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 Exchange Act) as of March 31, 2022. 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 Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports the Company files or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Changes in Internal Control over Financial Reporting

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, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. Other Information

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, 2022, we had an accumulated deficit of $684.7 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 $79.0 million in cash, cash equivalents and marketable securities as of March 31, 2022, along with net product revenues from product sales of FOTIVDA in the United States, would enable us to maintain our current operations for more than 12 months following the filing of this Quarterly Report on Form 10-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 in March 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;
- the impact of COVID-19 on our operations, business and prospects;
- our ability to establish and maintain strategic partnerships, licensing, collaboration 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 2020 Loan Facility (as defined below), 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, FOTIVDA and our future products, if any;
- and general economic, industry and market conditions, including, without limitation, the current adverse impact of the COVID-19 pandemic and political and economic instability caused by the current armed conflict between Russia and Ukraine and economic sanctions adopted in response to the conflict.

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 milestone specified in the 2020 Loan Facility that would allow us to access the remaining $5.0 million in available credit. We also expect to seek additional funds through arrangements with partners, licensees, collaborators 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 2020 Loan Facility and Hercules accelerates the then remaining principal payments and fees due under the 2020 Loan Facility, 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 governing our 2020 Loan Facility could result in an event of default, which could materially and adversely affect our business and our financial condition.

The Loan Agreement governing our 2020 Loan Facility includes certain financial and operational covenants and provides 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 would 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 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 only recently demonstrated our ability, or our ability to arrange for a third party, to manufacture a commercial scale medicine and conduct the sales and marketing activities necessary to commercialize a product. 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 FOTIVDA. In addition, as a relatively new commercial stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To be profitable, we will need to continue to successfully transition from a company with a research and development focus to a company capable of supporting commercial activities. Ultimately, we may not be successful in such a transition.

We rely on a limited number of key customers, the importance of which may vary dramatically from year to year, and a loss of one or more of these key customers may adversely affect our operating results.

Four customers accounted for approximately all of our net product revenues for FOTIVDA in the quarter ended March 31, 2022. One large specialty distributor accounted for 42% of our net product revenues for FOTIVDA in the quarter ended March 31, 2022, and we anticipate this customer will continue to be a significant contributor to our net product revenues for FOTIVDA for the remainder of 2022. The loss of a significant amount of business from one of our major customers would materially and adversely affect our results of operations until such time, if ever, as we are able to replace the lost business. Significant customers in any one period may not continue to be significant customers in other periods. In any given year, there is a possibility that a single specialty pharmacies and specialty distributors may account for 50% or more of our net product revenues for FOTIVDA. To the extent that we are dependent on any single customer, we are subject to the risks faced by that customer to the extent that such risks impede the customer's ability to stay in business and make timely payments to us.

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, which was acquired by Recordati in March 2022, in those countries outside the United States where FOTIVDA is currently approved. While we recorded a growing number of commercial prescriptions, factors beyond our control may result in decreases in commercial prescriptions each month or each quarter. If commercial prescription demand becomes stagnant or decreases it would substantially impact our revenues from product sales, adversely affect our profitability on a quarterly or annual basis and depress the market price of our common stock.

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 commercialize FOTIVDA in the United States;
- our ability to enhance commercial awareness of FOTIVDA;
- commercial acceptance by physicians, patients, third-party payors and others in the medical community;
- 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 trials, as well as that of our collaborators, investigator sponsors 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 continue 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.

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 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 FOTIVDA, 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 have required significant resources and may not ultimately be successful. Restrictions related to the ongoing COVID-19 pandemic have impeded our ability to gain in-person access to customers, prescribers, other healthcare professionals and to certain institutions that remain closed to industry representatives. We believe these access challenges caused by the COVID-19 pandemic and the emergence of SARs-CoV-2 variants have potentially slowed the commercial launch trajectory of FOTIVDA which we believe is causing a protracted launch curve as compared to the pre-COVID open access environment. While we have designed our strategic commercial approach to be optimized for remote as well as in-person customer engagement capabilities and expanded our digital marketing strategies in light of the restrictions necessitated by the COVID-19 pandemic, changes to standard sales and marketing practices, including the shift from in-person to video and virtual interactions with healthcare professionals, have caused, and may continue to cause, challenges for the successful commercialization of FOTIVDA.

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 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 marketing success of us as compared with our competitors;
- how the product is positioned in physician treatment guidelines and pathways;
- the prevalence and severity of any side effects;
- the efficacy and safety of the product;
- 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 of 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 prove to be inaccurate, the actual markets for our product candidate could be smaller than our estimates of the potential market opportunities.

If the FDA, EMA or other comparable foreign regulatory authorities approve generic versions of FOTIVDA®, the sales of FOTIVDA® could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labelling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. Specifically, in cases where such exclusivity has been granted, as is the case with FOTIVDA®, an ANDA may not be submitted to the FDA until the expiration of five years, e.g., March 10, 2026, for FOTIVDA®, unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug, *e.g.*, March 10, 2025, for FOTIVDA®.

Generic drug manufacturers may seek to launch generic products following the expiration of the applicable exclusivity period for FOTIVDA®, even if we still have patent protection for such products. Competition that FOTIVDA® could face from generic versions could materially and adversely affect our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in developing FOTIVDA®.

In addition to our dependence on the success of FOTIVDA, we depend on the success of our clinical stage assets, including tivozanib (in other indications), ficlatuzumab, AV-380 and AV-203. 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 European Medicines Agency, or 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. Despite our efforts to design satisfactory clinical trial protocols, we cannot guarantee that the clinical trial protocols of any of our ongoing clinical trials will satisfy the rigorous standards of the FDA and/or the EMA to support a marketing approval. If we seek to amend the clinical trial protocols for any of our clinical trials this may delay site enrollment and completion, as in the case of the TiNivo-2 Trial where we made a clinical trial protocol amendment. The TiNivo-2 trial protocol was amended based on (i) emerging evidence that the lower 0.89 mg dose was effective in combination with an ICI, (ii) that the lower dose may optimize the risk/benefit profile and result in better tolerability for the combination and (iii) the FDA's recommendation to investigate

an optimal dose of tivozanib in the combination setting under its Project Optimus initiative. We cannot be certain that this amendment to the TiNivo-2 protocol will satisfy the FDA's Project Optimus initiative to investigate the optimal dose of tivozanib in the combination setting and, if it does not, we may be required to conduct additional clinical trials which would delay and adversely impact the timing of marketing approval of tivozanib in combination with nivolumab or other therapies.

We depend heavily on the success of our clinical stage assets and our clinical trials may not be successful. If delays in manufacturing, trial site initiation or patient enrollment occur, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise, our clinical stage assets will develop at a slower pace than we had planned. For example, the delivery of the clinical supply of ficlatuzumab for a potential registrational clinical trial of ficlatuzumab in R/M HNSCC was significantly delayed due to the shortage of key raw materials and manufacturing supplies also used in COVID-19 vaccine manufacturing which required us to delay the start date of this potential registrational clinical trial until 2023.

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. For example, in December 2020, the FDA approved our investigational new drug, or IND, application for AV-380 for the potential treatment of cancer cachexia. In October 2021, we completed enrollment for a Phase 1 clinical trial in healthy subjects. Initial data observed a satisfactory reduction of GDF15 in subjects and no drug related adverse events were identified. However, operational errors at the trial site have caused data integrity concerns and we have notified the FDA. We plan to discuss with the FDA the suitability of the data for regulatory purposes and our ability to publish the data from this trial. We do not expect the data quality issues in the Phase 1 clinical trial to impact our plans to initiate a Phase 1b clinical trial in cancer patients in the second half of 2022. We cannot be certain that the data integrity concerns related to the Phase 1 clinical trial will not ultimately delay the development of our AV-380 program.

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;
- the supply or quality of raw materials, manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be significantly delayed, insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply, due to challenges related to the COVID-19 pandemic, global supply chain disruptions caused by the ongoing conflict between Russia and Ukraine or otherwise;
- 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, including GMPs, GCPs or GLPs, 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 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, or necessary supplies, 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 clinical 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 reassign 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 reassign 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 or limit 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;
- limited access to our customers due to the COVID-19 pandemic; 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 commercialization 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 commercialization of FOTIVDA and the continued development of 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/or 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. 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 acute myeloid leukemia, or 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, or 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.

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 evolving standard of care landscape;
- the proximity of patients to clinical sites;

- the design of and eligibility criteria for the 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 or any changes to the standard of care for the indications we are investigating. For example, changes in the standard of care in HCC have extended treatment time with first line therapies and reduced the presence of a sufficient patient pool suitable for the DEDUCTIVE trial, which has delayed patient enrollment for the trial.

If approved, our product candidates, such as ficlatuzumab, AV-380, or AV-203, that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, or the ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, our antibody product candidates, for example, ficlatuzumab, AV-380 or AV-203, if approved by the FDA, would benefit from 12 years of data exclusivity from the time of first licensure. While the FDA could not accept an application for a biosimilar or interchangeable product based on our biologic product candidates, such as ficlatuzumab, AV-380 or AV-203, as the reference biological product until four years after the date of first licensure of our product candidate, during this 12-year period of exclusivity, another party may still independently develop and receive approval of a competing biologic, so long as its BLA does not rely on our product candidate's data or submit the application as a biosimilar application. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty, and any new policies or processes adopted by the FDA could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the biological product candidates we develop under a BLA, such as ficlatuzumab, AV-380 or AV-203, should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. Nonetheless, the approval of a biosimilar to our biologic product candidates, such as ficlatuzumab, AV-380 or AV-203, would have a material adverse impact on our business due to increased competition and pricing pressure.

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 and maintain 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 working to secure reimbursement approval for and commercially launch FOTIVDA in many of the countries in which FOTIVDA has been approved. However, there is significant competition in the first-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, or reimbursement is limited, and if EUSA is unable to commercially launch FOTIVDA in additional 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 of the United States. 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 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, 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 or interruption 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. Our 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 cyber incidents, misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including commercial information and personal information of our employees, patients, clinical trial participants and third-party vendors.

System failures, accidents, cyber incidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our commercialization and clinical 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 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 commercialize FOTIVDA by restricting in-person access to treating oncologists and restricting in-person access to certain institutions, our ability to initiate new trials or complete ongoing clinical trials and our ability to manufacture clinical product and may have other 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 manufacturing materials, 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.

Restrictions related to the ongoing COVID-19 pandemic have impeded our ability to gain in-person access to customers, prescribers, and other healthcare professionals and certain institutions remain closed to industry representatives. We believe these access challenges caused by the COVID-19 pandemic and the emergence of SARs-CoV-2 variants have potentially slowed the commercial launch trajectory of FOTIVDA which we believe is causing a protracted launch curve as compared to the pre-COVID open access environment. While we have designed our strategic commercial approach to be optimized for remote as well as in-person customer engagement capabilities and expanded our digital marketing strategies in light of the restrictions necessitated by the COVID-19 pandemic, changes to standard sales and marketing practices, including the shift from in-person to video and virtual interactions with healthcare professionals, have caused, and may continue to cause, challenges for the successful commercialization of FOTIVDA.

The COVID-19 pandemic has also impacted the initiation, enrollment and completion of certain of our ongoing and planned clinical trials both in the United States and in the EU. For example, the pandemic partially slowed enrollment of the DEDUCTIVE trial in that it hindered patients' ability to attend routine physical medical assessments with their clinicians resulting in delays in diagnosis and, at times, treatment of cancer in patients. In addition, in-person monitoring visits are currently on hold at certain of the active clinical trial sites for 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.

Similarly, the CRO for our TiNivo-2 trial has been impacted by cancer research staffing shortages related to, among other things, COVID-19 infections and competition for staff at clinical trial sites resulting in delays to site initiation, contracting and enrollment. Currently, certain academic institutions have frozen enrollment on all trials or refused to take on additional clinical trials due to these staffing shortages and these staffing shortages have adversely impacted trial site initiation and enrollment of the TiNivo-2 trial.

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, including manufacturing supplies, 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 CMO 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.

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.

Any negative impact that the COVID-19 pandemic has on the ability of our suppliers to provide materials for our product candidates could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to initiate or complete clinical trials, 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. For example, the COVID-19 pandemic has, and may continue to, cause delays in the manufacturing of our product candidates ficlatuzumab and AV-380. A shortage of required key raw materials and manufacturing supplies also used in COVID-19 vaccine manufacturing process delayed the delivery of the clinical supply of ficlatuzumab originally expected in the first half of 2022 and required us to delay the start date of this potential registrational clinical trial until the first half of 2023, which, if approved, may impact timing of potential commercialization and associated revenue generation. Similarly, a separate CMO has experienced employee shortages, supply chain issues and disruptions related to the COVID-19 pandemic which has delayed and may continue to delay manufacturing of AV-380. While we believe there are alternate manufacturers with capability to supply clinical or, if approved, commercial supply of AV-380 necessary to meet our needs, contracting with additional CMOs would require significant lead-times and result in additional costs and currently is not the solution we expect to follow.

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, the supply chain, 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. The macroeconomic impacts arising from the duration of the COVID-19 pandemic, including supply chain disruptions, may have prolonged and unforeseen adverse impacts to our industry, business and operations. In addition, this pandemic has adversely impacted economies worldwide and may cause additional disruption in the financial markets, both of which could result in adverse effects on our business, operations and ability to raise capital.

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 GCPs and GLPs 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. 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. For example, the third-party CRO that conducted our AV-380 Phase 1 clinical trial evaluating the safety of AV-380 in healthy subjects failed to comply with regulatory requirements applicable to the clinical trial, including GCPs and GLPs, which resulted in data integrity concerns. We have notified the FDA and plan to discuss the errors that occurred at the trial site with the FDA to confirm whether we will be able to publish the data from this trial and the suitability of the data for regulatory purposes. If the FDA determines that the data from the clinical trial is not suitable for use, our development of AV-380 may be delayed.

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 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 timely produce or provide required manufacturing supplies for us or to safely store product candidate supplies and commercial supplies of FOTIVDA may delay or impair our ability to manufacture product, initiate or 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, many of whom have experienced delays and challenges related to the COVID-19 pandemic. Such suppliers may not be able to provide these materials to our manufacturers at the times we need them or on commercially reasonable terms. For example, the delivery of the clinical supply of ficlatuzumab for a potential registrational clinical trial of ficlatuzumab in R/M HNSCC was significantly delayed due to the shortage of key raw materials and manufacturing supplies also used in COVID-19 vaccine manufacturing, which required us to delay the start date of this potential registrational clinical trial until 2023. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers and delays related to the COVID-19 pandemic to provide raw and starting materials that we use to manufacture our product candidates could delay or disrupt our ability to initiate or continue clinical trials on our scheduled timelines or at all, which may impact timing of potential commercialization and associated revenue generation.

More recently, one of our CMOs has experienced employee shortages, supply chain issues and disruptions related to the COVID-19 pandemic which have delayed and may continue to delay manufacturing of AV-380 preclinical supply. Any significant delay in the supply of a product candidate or the raw material components thereof for a scheduled or 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 such as the disruption to the supply chain caused by the COVID-19 pandemic. If our product candidate supplies or commercial supplies of FOTIVDA were lost, destroyed, significantly delayed or otherwise compromised, it would delay or impair our ability to complete clinical trials and commercialize FOTIVDA.

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

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. In March 2022, EUSA was acquired by Recordati. As a result of the acquisition, all rights and obligations under the EUSA Agreement are transferred to Recordati. We have limited contractual rights to force Recordati to invest significantly in the commercialization of FOTIVDA in jurisdictions covered by the EUSA Agreement. For instance, under the EUSA Agreement, Recordati, and formerly 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 Recordati, fails to adequately commercialize FOTIVDA because it lacks adequate financial or other resources, decides to focus on other initiatives or

otherwise, our ability to successfully commercialize FOTIVDA in the applicable jurisdictions would be limited, which may 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 Recordati 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 revenue from sales of FOTIVDA outside the United States would be materially harmed.

While EUSA attempted to secure reimbursement approval in and commercially launch FOTIVDA in additional countries in the EUSA Licensed Territory, there is significant competition in the first-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 and Recordati will likely face similar obstacles as it seeks to secure reimbursement approval and commercially launch FOTIVDA in additional countries in the EUSA Licensed Territory. If Recordati, is unable to secure reimbursement approval in and commercially launch FOTIVDA in additional countries in the EUSA Licensed Territory 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.

Further, we cannot be certain that Recordati leadership will prioritize reimbursement approval and commercially launching FOTIVDA in additional countries in the EUSA Licensed Territory. If the integration of EUSA into Recordati's organization is slow or unsuccessful or the Recordati leadership does not seek to prioritize reimbursement approval and/or a commercial launch of FOTIVDA in additional countries in the EUSA Licensed Territory, 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, regulatory filings, 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. 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. 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 Life Sciences, Ltd 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 collaboration and license agreement for convenience. The transfer of the AV-203 program occurred in September 2021, which has delayed the initiation of clinical trials of AV-203 even further.

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.

Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a natural disaster, pandemic, war or other catastrophic event.

We depend on our employees, consultants, CMOs, CROs, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions we take for natural disasters or other catastrophic events, these events, including terrorist attacks, pandemics, hurricanes, fires, floods and ice and snowstorms, could result in significant disruptions to our research and development, preclinical studies, clinical trials, and, ultimately, commercialization of our products. Long-term disruptions in the infrastructure caused by events, such as natural disasters, the outbreak of war (including expansion of the current armed conflict between Russia and Ukraine), the escalation of hostilities and acts of terrorism or other "acts of God," particularly involving cities in which we have offices, manufacturing or clinical trial sites, could adversely affect our businesses. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not include or be adequate to compensate us for all losses that may occur. Any natural disaster or catastrophic event affecting us, our CMOs, our CROs, regulatory agencies or other parties with which we are engaged could have a material adverse effect on our operations and financial performance.

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 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, inclusive of a one year interim extension granted by the USPTO, is scheduled to expire in April 2023, and a second U.S. patent covering the crystalline form of tivozanib, which is scheduled to expire in November 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 have applied 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, Sweden and the United Kingdom, 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 application for an SPC on the patent covering the tivozanib molecule in Denmark 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, with respect to FOTIVDA, generic manufacturers could challenge the patents covering FOTIVDA 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. Further, 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.

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.

Tivozanib and certain of our product candidates 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. Outside parties have in the past penetrated and may in the future 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. We monitor our systems closely and continue to seek to improve our cybersecurity capacities to minimize hacking efforts by various outsides parties. Like other companies, we have experienced and may in the future 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. The risk of cyber incidents could also be increased by cyberwarfare in connection with the ongoing conflict between Russia and Ukraine, including potential proliferation of malware from the conflict into systems unrelated to the conflict. 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.

The number and complexity of these security threats continue to increase over time. If a breach of our security systems 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 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 marketing 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 market and 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.

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. 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 or our collaborators may not obtain marketing approvals from regulatory authorities outside the United States on a timely basis, if at all, and we may not receive necessary approvals to commercialize our products in any particular market.

In many countries outside the United States, a product candidate must be approved for reimbursement before the product can be approved for sale 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 withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the EU. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

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 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 clinical 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.

We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the US, and PRIME Designation in the EU, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that product candidate will receive marketing approval.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product’s application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective.

For example, we have been granted Fast Track designation for the investigation of ficlatuzumab and cetuximab for the treatment of patients with relapsed or recurrent HNSCC. Marketing applications filed by sponsors of product candidates in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. Even though we have received Fast Track designation for ficlatuzumab and cetuximab, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track

designation if it believes that the designation is no longer supported by data from our clinical development program. Further, the FDA may withdraw Fast Track designation at any time. As such, a Fast Track designation by the FDA, even though granted for ficlatuzumab may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that ficlatuzumab will receive marketing approval.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

In the EU, we may seek PRIME designation for our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the EU or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the EU and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims.

The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

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 in the United States and EU, 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 the EU. 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 our 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.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the Agency to mean the "indication or use." We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates 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 and the SEC, have had to furlough critical FDA, SEC and other government 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. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. Following a period of false starts, the FDA announced, on February 2, 2022, that it would resume domestic inspections beginning on February 7, 2022. As for foreign jurisdictions, the FDA indicated that it would continue planned inspections in countries that have received country clearance and are within the CDC's level 1 or level 2 COVID-19 travel recommendation. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption 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. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

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.

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 are restricted from promoting 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.

Similar restrictions apply to the approval of our products in the EU. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the EU's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the EU and are also subject to EU Member State laws. 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.

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 laws 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. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations involve substantial costs.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations 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 business practices or operations are found to be in violation of any of the laws described above, other or future healthcare laws or case law or any 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. 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. Further, 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, which could impact us.

Any relationships we may have with customers, healthcare providers and professionals and third-party payors, among others, will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for or the purchase, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid.

False Claims Laws. The federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions against individuals or entities for, among other things, knowingly presenting or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties.

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing a scheme or making materially false statements in connection with the delivery of or payment for health care benefits, items or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or transfers of value made to physicians, other healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians, other healthcare providers and their immediate family members.

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that any business arrangements we have with third parties and our business generally, 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, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU member states. In addition, payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU member states. These requirements are provided in the national laws,

industry codes or professional codes of conduct, applicable in the EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.

As a condition of reimbursement by various federal and state health insurance programs, biotechnology and pharmaceutical companies are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as the courts. We have made reasonable assumptions where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. We are required to report any revisions to our calculations, price reporting and payment obligations previously reported or paid. Such revisions could affect liability to federal and state payers and also adversely impact our reported financial results of operations in the period of such restatement.

Uncertainty exists as new laws, regulations, judicial decisions or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If we become subject to investigations, restatements or other inquiries concerning compliance with price reporting laws and regulations, we could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on our business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of products and thus have an adverse impact on our financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in a company having to carry a liability on its consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than our current estimates, our financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if we are found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to the Centers for Medicare & Medicaid Services, or CMS, we may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreements, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for covered outpatient drugs.

Additionally, if we were found to have overcharged the government in connection with the FSS program or TriCare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, we would be required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges could result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our collaborators are also subject to similar requirements outside of the U.S. and thus the attendant risks and uncertainties. If our collaborators suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material and adverse impact on our revenues.

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 heard this case on November 10, 2020 and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. 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 pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that tie Medicare Part B payments for certain physician-administered pharmaceuticals to lower prices paid in other economically advanced countries, effective January 1, 2021. The rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration until January 1, 2026 by the Infrastructure Investment and Jobs Act. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 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. 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. 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, expensive and time-consuming 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 EU activities.

Given the breadth and depth of the GDPR and changes in data protection obligations, preparing for and complying with these requirements is rigorous, expensive and time-consuming 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 participants, 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. 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. 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 proper 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. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us and we could incur significant costs associated with environmental liability or toxic tort claims for failure to comply with such laws and regulations.

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 attainment of regulatory approvals and successful 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/or 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 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 manufacturing or 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 supply chain, manufacturing timelines, 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, including the recent sell off in the stock market for many companies 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. 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 elsewhere in this section "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, as a stockholder, you rely 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 litigation in which we may become involved;
- changes in our 2020 Loan Facility, 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 experienced extreme volatility and disruptions since 2020 due to the COVID-19 pandemic and the government measures taken in response to the pandemic and more recently due to inflationary pressures in the United States and the uncertainty surrounding ongoing geopolitical tensions and trade wars. 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, 2022, we had approximately $79.0 million of cash, cash equivalents and marketable securities consisting of cash on deposit with banks and in a U.S. government money market fund, and high-grade debt securities, including commercial paper, and U.S. government agency securities. 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, 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. The exercise of these options 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. In addition, our independent registered public accounting firm has attested 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 2020 Loan Facility 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 Coronavirus Aid, Relief, and Economic Security Act, or 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, 2021, we had federal net operating loss carryforwards of $613.1 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 $12.6 million, which will, if not used, expire at various dates through 2041. 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. As of December 31, 2021, we have recorded a full valuation allowance to offset these deferred tax assets because the future realizability of such assets is uncertain.

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.

Exhibit Index

ibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
Third Amendment to Amended and Restated Loan and Security Agreement, dated March 8, 2022, by and among the Registrant, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc.		10-K	001-34655	03/14/2022	10.32	
Office Lease dated April 4, 2022, by and between Registrant and TFC 30 Winter, LLC		8-K	001-34655	04/04/2022	99.1	
Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.						X
Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.						X
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
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
XBRL Instance Document.						X
XBRL Taxonomy Extension Schema Document.						X
XBRL Taxonomy Calculation Linkbase Document.						X
XBRL Taxonomy Extension Definition Linkbase Document.						X
XBRL Taxonomy Label Linkbase Document.						X
XBRL Taxonomy Presentation Linkbase Document.						X
Cover Page Interactive Data File (embedded within the Inline XBRL document).						

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 5, 2022 By: /s/ Erick Lucera

Erick Lucera

Chief Financial Officer and Principal Financial And Accounting Officer

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 5, 2022

/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 5, 2022

/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, 2022 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 5, 2022

/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, 2022 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 5, 2022

/s/ Erick Lucera

Erick Lucera
Chief Financial Officer
(Principal Financial Officer)