AVEO PHARMACEUTICALS INC
Form 10-Q
August 04, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-Q

(Mark One)

x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended June 30, 2016

OR

o 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.)

One Broadway, 14th Floor, Cambridge, Massachusetts 02142

(Address of Principal Executive Offices) (Zip Code)

(617) 588-1960

(Registrant's Telephone Number, Including Area Code)

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 x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes x No ¨

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

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

Number of shares of the registrant's Common Stock, $0.001 par value, outstanding on July 29, 2016: 75,859,613

AVEO PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE QUARTER ENDED JUNE 30, 2016

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets

(In thousands, except par value amounts)

(Unaudited)

	June 30, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$25,331	$26,634
Marketable securities	14,200	7,501
Accounts receivable	1,302	4,641
Other prepaid expenses and other current assets	1,421	1,600
Total current assets	42,254	40,376
Property and equipment, net	22	23
Other assets	410	143
Total assets	$42,686	$40,542
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$2,079	$1,425
Accrued contract research	2,772	1,966
Other accrued liabilities	1,453	2,140
Loans payable, net of discount	—	2,053
Deferred revenue	660	814
Settlement liability (Note 11)	—	4,000
Total current liabilities	6,964	12,398
Loans payable, net of current portion and discount	13,735	7,418
Deferred revenue	2,666	2,881
Warrant liability (Note 7)	10,340	—
Other liabilities	690	618
Total liabilities	34,395	23,315
Stockholders' equity:		
Preferred stock, $.001 par value: 5,000 shares authorized; no shares issued and Outstanding		—
Common stock, $.001 par value: 200,000 shares authorized; 75,860 and 58,182 shares issued and outstanding at June 30, 2016 and December 31, 2015, respectively	76	58
Additional paid-in capital	519,550	512,201
Accumulated other comprehensive income (loss)	10	(3)

Accumulated deficit	(511,345)	(495,029)
Total stockholders' equity	8,291	17,227
Total liabilities and stockholders' equity	$42,686	$40,542

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations

(In thousands, except per share amounts)

(Unaudited)

	Three Months Ended		Six Months Ended	
	June 30, 2016	2015	June 30, 2016	2015
Collaboration and licensing revenue	$193	$134	$1,396	$268
Operating expenses:				
Research and development	5,604	1,841	11,576	4,536
General and administrative	1,731	2,889	4,203	6,144
Restructuring and lease exit	—	25	—	4,358
	7,335	4,755	15,779	15,038
Loss from operations	(7,142)	(4,621)	(14,383)	(14,770)
Other expense, net:				
Interest expense, net	(468)	(626)	(837)	(1,337)
Change in fair value of warrant liability	(996)	—	(996)	—
Other expense	—	(209)	—	(223)
Other expense, net	(1,464)	(835)	(1,833)	(1,560)
Loss before provision for income taxes	(8,606)	(5,456)	(16,216)	(16,330)
Provision for income taxes	—	—	(100)	—
Net loss	$(8,606)	$(5,456)	$(16,316)	$(16,330)
Net loss per share basic and diluted	$(0.13)	$(0.10)	$(0.26)	$(0.30)
Weighted average number of common shares outstanding	66,917	55,164	62,566	53,908

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss

(In thousands)

(Unaudited)

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2016	2015	2016	2015
Net loss	$(8,606)	$(5,456)	$(16,316)	$(16,330)
Other comprehensive income (loss):				
Unrealized gain (loss) on available-for-sale securities	8	—	13	—
Comprehensive loss	$(8,598)	$(5,456)	$(16,303)	$(16,330)

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

AVEO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows

(In thousands)

(Unaudited)

	Six Months Ended June 30,	
	2016	2015
Operating activities		
Net loss	$ (16,316)	$ (16,330)
Adjustments to reconcile net loss to net cash used in operating activities:		
Impairment of property and equipment	—	232
Depreciation and amortization	7	9,464
Accretion	—	224
Loss on disposal of fixed assets	—	245
Stock-based compensation	624	838
Non-cash interest expense	196	244
Non-cash change in fair value warrant liability	996	—
Amortization of premium and discount on investments	13	33
Changes in operating assets and liabilities:		
Restricted cash	—	135
Accounts receivable	3,339	21
Prepaid expenses and other current assets	179	56
Other noncurrent assets	(267)	51
Accounts payable	656	(1,678)
Accrued contract research	806	(4,184)
Other accrued liabilities	(695)	(559)

Settlement liability	(4,000)	—
Deferred revenue	(369)	(153)
Lease exit obligation	—	(5,205)
Deferred rent	—	(10,569)
Other liabilities	(78)	(115)
Net cash used in operating activities	(14,909)	(27,250)
Investing activities		
Purchases of marketable securities	(19,949)	(8,808)
Proceeds from maturities and sales of marketable securities	13,250	8,775
Proceeds from sale of property and equipment	—	1,221
Net cash (used in) provided by investing activities	(6,699)	1,188
Financing activities		
Proceeds from issuance of common stock and warrants, net of issuance costs	14,862	5,840
Proceeds from issuance of common stock and warrants to related parties	525	—
Proceeds from issuance of loan payable and warrants	5,000	—
Proceeds from exercise of stock options and issuance of common and restricted stock	33	275
Debt issuance costs	(115)	—
Principal payments on loans payable	—	(5,593)
Net cash provided by financing activities	20,305	522
Net decrease in cash and cash equivalents	(1,303)	(25,540)
Cash and cash equivalents at beginning of period	26,634	52,306
Cash and cash equivalents at end of period	$ 25,331	$ 26,766
Supplemental cash flow information		

Cash paid for interest	$	631	$	1,162
Non-cash financing activity				
Fair value of warrants issued in connection with long term debt	$	667	$	—
Fair value of warrants issued in connection with private placement	$	9,344	$	—

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

AVEO Pharmaceuticals, Inc.

Notes to Condensed Consolidated Financial Statements

(Unaudited)

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. The Company's proprietary platform has delivered unique insights into cancer and related disease. The Company's strategy is to leverage these biomarker insights and partner resources to advance the development of its clinical pipeline.

The Company's pipeline of product candidates includes tivozanib, a potent, selective, long half-life vascular endothelial growth factor tyrosine kinase inhibitor of all three vascular endothelial growth factors. In June 2013, the U.S. Food and Drug Administration issued a complete response letter denying the Company's application for approval of the use of tivozanib in first-line treatment of advanced renal cell carcinoma ("RCC"), citing concerns regarding the negative trend in overall survival in the Company's pivotal phase 3 trial. In May 2016, the Company initiated enrollment and treatment of patients in a new phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC in order to address the overall survival concerns presented in the June 2013 complete response letter from the FDA and to support a request for regulatory approval of tivozanib in the United States as a third-line treatment and as a first-line treatment. The Company is also planning a phase 1/2 trial of tivozanib in combination with an immune checkpoint (PD-1) inhibitor for the treatment of RCC. In February 2016, a strategic partner submitted a Marketing Authorization Application for tivozanib with the European Medicines Agency ("EMA") for the treatment of RCC. The application was validated in March 2016, confirming that the submission was complete and that the EMA would initiate its review process. The Company's partner received the Day 120 List of Questions from the EMA on July 21, 2016.

The Company also has a pipeline of monoclonal antibodies, including:

(i) Ficlatuzumab, a potent anti-HFG antibody that inhibits the activity of the HGF/c-Met pathway and for which the Company has completed a phase 2 clinical trial and has entered into a partnership with Biodesix, Inc. ("Biodesix") to advance clinical development;

(ii) AV-203, a potent, high affinity inhibitor of ErbB3 function that has demonstrated anti-tumor activity in multiple preclinical models and for which the Company has completed a phase 1 dose escalation trial and has entered into a partnership with CANbridge Life Sciences Ltd. ("CANbridge") to advance clinical and manufacturing development;

(iii) AV-380, a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment or prevention of cachexia, which the Company has licensed to Novartis International Pharmaceutical Ltd. ("Novartis"); and

(iv) AV-353, a potent inhibitory antibody specific to Notch 3, which has demonstrated an ability in preclinical models to potentially reverse disease phenotype for pulmonary arterial hypertension ("PAH"), and for which the Company is currently seeking a partner to advance development in PAH.

As used throughout these condensed consolidated financial statements, the terms "AVEO," and the "Company" refer to the business of AVEO Pharmaceuticals, Inc. and its two wholly-owned subsidiaries, AVEO Pharma Limited and AVEO Securities Corporation.

The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property

and general and administrative functions relating to these operations.

The Company has an accumulated deficit as of June 30, 2016 of approximately $511.3 million and is subject to a number of risks, including the need for substantial additional capital for clinical research and product development and the requirement to maintain compliance with its financial covenant pursuant to its loan and security agreement (refer to Note 6). The Company will need additional funding to support its planned operating activities, and the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

(2) Basis of Presentation

These condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, AVEO Pharma 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 generally accepted accounting principles (GAAP) for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by generally accepted accounting principles 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 and six months ended June 30, 2016 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2016 or any other future period.

The information presented in the condensed consolidated financial statements and related footnotes at June 30, 2016, and for the three months and six months ended June 30, 2016 and 2015, is unaudited, and the condensed consolidated balance sheet amounts and related footnotes as of December 31, 2015 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, 2015, which was filed with the U.S. Securities and Exchange Commission ("SEC") on March 15, 2016.

Certain reclassifications have been made to prior periods to conform to current period presentation. Reclassification of prior year amounts has been made to separately present accrued contract research from accrued expenses on the consolidated balance sheets and to present interest expense net of interest income on the consolidated statements of operations. There was no impact on total liabilities, total other expenses or net income (loss) resulting from these reclassifications.

(3) Significant Accounting Policies

Revenue Recognition

The Company's revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple elements, or deliverables, 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 pre-clinical and clinical material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, up-front license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

When evaluating multiple element arrangements, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables within each agreement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available. Determining the best estimate of selling price for a deliverable requires significant judgment. The Company typically uses best estimate of selling price to estimate the selling price for licenses to the Company's proprietary technology, since the Company often does not

have VSOE or TPE of selling price for these deliverables. In those circumstances where the Company utilizes best estimate of selling price to determine the estimated selling price of a license to the Company's proprietary technology, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements and internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the Company's best estimate of selling price, the Company evaluates whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration among multiple deliverables.

The Company typically receives non-refundable, up-front payments when licensing its intellectual property in conjunction with a research and development agreement. When management believes the license to its intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, the Company generally recognizes revenue attributed to the license on a straight-line basis over the Company's contractual or estimated performance period, which is typically the term of the Company's research and development obligations. If management cannot reasonably estimate when the Company's performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. When management believes the license to its intellectual property has stand-alone value, the Company generally recognizes revenue attributed to the license upon delivery. The periods over which revenue should be recognized are subject to estimates by management

and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Payments or reimbursements resulting from the Company's research and development efforts for those arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured. Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets.

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment.

The Company aggregates its milestones into four categories: (i) clinical and development milestones, (ii) regulatory milestones, (iii) commercial milestones, and (iv) patent-related milestones. Clinical and development milestones are typically achieved when a product candidate advances into a defined phase of clinical research or completes such phase. For example, a milestone payment may be due to the Company upon the initiation of a phase 3 clinical trial for a new indication, which is the last phase of clinical development and could eventually contribute to marketing approval by the U.S. Food and Drug Administration ("FDA") or other global regulatory authorities. Regulatory milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other global regulatory authorities. For example, a milestone payment may be due to the Company upon the FDA's acceptance of a New Drug Application ("NDA"). Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount. Patent-related milestones are typically achieved when a patent application is filed or a patent is issued with respect to certain intellectual property related to the applicable collaboration.

Revenues from clinical and development, regulatory, and patent-related milestone payments, if the milestones are deemed substantive and the milestone payments are nonrefundable, are recognized upon successful accomplishment of the milestones. The Company has concluded that the clinical and development, regulatory and patent-related milestones pursuant to its current research and development arrangements are substantive. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance. Revenues from commercial milestone payments are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

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 personnel-related costs such as salaries and stock-based compensation, facilities, research-related overhead, clinical trial costs, manufacturing costs and costs of other contracted services, license fees, and other external costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received.

Warrants Issued in Connection with Private Placement

The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. These warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a non-cash component of other expense, until the earlier of their exercise or expiration or upon the completion of a liquidation event.

During the three months ended June 30, 2016, as a result of the fair value adjustment of the warrant liability, the Company recorded a non-cash loss on the increase in the fair value of approximately $1.0 million, in its Statements of Operations and

Comprehensive Income (Loss). Refer to Note 7, “Common Stock - Private Placement” for further discussion on the calculation of the fair value of the warrant liability.

The following table rolls forward the fair value of the Company’s warrant liability, the fair value of which is determined by Level 3 inputs for the six months ended June 30, 2016 (in thousands):

	Six Months Ended June 30, 2016
Fair value, beginning of period	$—
Issuance of warrants	9,344
Exercise of warrants	—
Non-cash loss (gain) from change in fair value	996
Fair value, end of period	$10,340

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 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 money market funds and high-grade, short-term commercial paper, corporate bonds and U.S. 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.

Marketable Securities

Marketable securities consist primarily of investments which have expected average maturity dates in excess of three months, but not longer than 24 months. The Company invests in high-grade corporate obligations, including commercial paper, and U. S. 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 to maturity, 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. There were no realized gains or losses recognized on the sale or maturity of marketable securities during the three months and six months ended June 30, 2016 and 2015.

Below is a summary of cash, cash equivalents and marketable securities at June 30, 2016 and December 31, 2015:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
June 30, 2016:				
Cash and cash equivalents:				
Cash and money market funds	$15,331	$ —	$ —	$15,331
Government agency securities	505	—	—	505
Corporate debt securities	9,495	—	—	9,495
Total cash and cash equivalents	25,331	—	—	25,331
Marketable securities:				
Corporate debt securities due within 1 year	9,834	2	—	9,836
Government agency securities due within 1 year	4,356	8	—	4,364
Total marketable securities	14,190	10	—	14,200
Total cash, cash equivalents and marketable securities	$39,521	$ 10	$ —	$39,531
December 31, 2015:				
Cash and cash equivalents:				
Cash and money market funds	$21,822	$ —	$ —	$21,822
Corporate debt securities	4,812	—	—	4,812
Total cash and cash equivalents	26,634	—	—	26,634
Marketable securities:				
Corporate debt securities due within 1 year	$6,504	$ —	$ (3)	$6,501
Government agency securities due within 1 year	1,000	—	—	1,000
Total marketable securities	7,504	—	(3)	7,501
Total cash, cash equivalents and marketable securities	$34,138	$ —	$ (3)	$34,135

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 accounts receivable primarily consists of amounts due to the Company from licensees and collaborators. As of June 30, 2016, the Company had $1.3 million of accounts receivable outstanding, primarily

due from Biodesix pursuant to the Company's collaboration arrangement for AV-299 of which approximately $0.8 million was received in July 2016 (refer to Note 4). The Company has not experienced any material losses related to accounts receivable 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 June 30, 2016, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a money market fund and its financial assets valued based on Level 2 inputs consisted of high-grade corporate bonds, commercial paper and U.S. government agency securities. During the three months and six months ended June 30, 2016, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of June 30, 2016, the Company's financial liabilities that were recorded at fair value consisted of a warrant liability.

The fair value of the Company's loans payable at June 30, 2016 approximates its carrying value, computed pursuant to a discounted cash flow technique using a market interest rate and is considered a Level 3 fair value measurement. The effective interest rate, which reflects the current market rate, considers the fair value of the warrants issued in connection with the loan, loan issuance costs and the deferred financing charge.

The following table summarizes the assets and liabilities measured at fair value on a recurring basis at June 30, 2016 and December 31, 2015:

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of June 30, 2016

	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash equivalents	$15,331	$—	$—	$15,331
Corporate debt securities	—	9,495	—	9,495
Government agency securities	—	505	—	505
Total cash and cash equivalents	$15,331	$10,000	$—	$25,331
Marketable securities:				
Corporate debt securities due within 1 year	$—	$9,836	$—	$9,836
Government agency securities due within 1 year	—	4,364	—	4,364
Total marketable securities	$—	$14,200	$—	$14,200
Tota cash, cash equivalents and marketable securities	$15,331	$24,200	$—	$39,531
Financial liabilities carried at fair value:				
Warrant liability	$—	$—	$10,340	$10,340
Total warrant liability	$—	$—	$10,340	$10,340

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2015			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash equivalents	$21,822	$—	$ —	$21,822
Corporate debt securities	—	4,812		4,812
Total cash and cash equivalents	$21,822	$4,812	$ —	$26,634
Marketable securities:				
Corporate debt securities due within 1 year	$—	$6,501	$ —	$6,501
Government agency securities due within 1 year	—	1,000	—	1,000
Total marketable securities	$—	$7,501	$ —	$7,501
Tota cash, cash equivalents and marketable securities	$21,822	$12,313	$ —	$34,135
Financial liabilities carried at fair value:				
Warrant liability	$—	$—	$ —	$—
	$—	$—	$ —	$—

Property and Equipment

Property and equipment are stated at cost and are depreciated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repair costs are charged to expense as incurred. During the quarter ended June 30, 2015, the Company transitioned to new office space and, as a result, revised the estimated useful life of its office furniture, resulting in an increase in depreciation expense of approximately $0.4 million during the three months and six months ended June 30, 2015, respectively.

Long-lived Assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever changes in business circumstances indicate that the carrying amount of the asset may not be fully recoverable. No impairment charges were recognized during the three months and six months ended June 30, 2016. The Company recognized $0.2 million of impairment from losses for the six months ended June 30, 2015 related to leasehold improvements.

Basic and Diluted Loss per Common Share

Basic loss per share is computed by dividing net loss available to common stockholders by the weighted-average number of common shares outstanding during the period. Diluted loss per share is computed by dividing net loss available to common stockholders by the weighted-average number of common shares and dilutive common share equivalents then outstanding which excludes unvested restricted stock. Potential common share equivalents consist of the incremental common shares issuable upon the exercise of stock options and warrants. Since the Company had a net loss for all periods presented, the effect of all potentially dilutive securities is anti-dilutive. Accordingly, basic and diluted net loss per common share is the same.

The following table sets forth the potential common shares excluded from the calculation of net loss per common share-diluted for the three months and six months ended June 30, 2016 and 2015 because their inclusion would have

been anti-dilutive:

	Outstanding at June 30,	
	2016	2015
	(in thousands)	
Options outstanding	5,828	6,420
Warrants outstanding	19,453	609
	25,281	7,029

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 all awards is recognized in the Company's statements of operations over the requisite service period for each award.

Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. Other awards, such as performance-based awards that vest upon the achievement of specified goals, are expensed using the accelerated attribution method if achievement of the specified goals is considered probable. The Company has also granted awards that vest upon the achievement of market conditions. Per Accounting Standards Codification ("ASC") 718 Share-Based Payments, market conditions must be considered in determining the estimated grant-date fair value of share-based payments and the market conditions must be considered in determining the requisite service period over which compensation cost is recognized. The Company estimates the fair value of the awards with market conditions using a Monte Carlo simulation, which utilizes several assumptions including the risk-free interest rate, the volatility of the Company's stock and the exercise behavior of award recipients. The grant-date fair value of the awards is then recognized over the requisite service period, which represents the derived service period for the awards as determined by the Monte Carlo simulation.

The fair value of equity-classified awards to employees and directors are measured at fair value on the date the awards are granted. Awards to nonemployee consultants are recorded at their fair values and are re-measured as of each balance sheet date until the recipient's services are complete. During the three months and six months ended June 30, 2016 and 2015, the Company recorded the following stock-based compensation expense:

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2016	2015	2016	2015
	(in thousands)		(in thousands)	
Research and development	$56	$63	$182	$188
General and administrative	177	348	442	581
Restructuring	—	—	—	69
	$233	$411	$624	$838

Stock-based compensation expense is allocated to research and development and general and administrative expense based upon the department of the employee to whom each award was granted. Expenses recognized in connection with the modification of awards in connection with the Company's strategic restructurings are allocated to restructuring expense. No related tax benefits of the stock-based compensation expense have been recognized.

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 June 30, 2016, the Company is forecasting a net loss for the year ended December 31, 2016. The Company maintains a full valuation allowance on all deferred tax assets. For the six months ended June 30, 2016, the Company recorded a $0.1 million provision for income taxes related to withholding taxes incurred in a foreign jurisdiction.

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 June 30, 2016, the Company has $0.9 million of net assets located in the United Kingdom.

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, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include contract research accruals and measurement of stock-based compensation. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Recent Accounting Pronouncements

The Company did not adopt any new accounting pronouncements during the six months ended June 30, 2016 that had a material effect on the Company's condensed consolidated financial statements.

In May 2014, the Financial Accounting Standards Board ("FASB") issued a comprehensive new revenue recognition standard that will supersede nearly all existing revenue recognition guidance under US GAAP. The standard was originally scheduled to be effective for public entities for annual and interim periods beginning after December 15, 2016. In July 2015, the standard was deferred and will now be effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted for annual and interim periods beginning after December 15, 2016. The Company is currently evaluating the effect this standard will have on its revenue recognition policies and its financial statements, including how the standard will be adopted.

In August 2014, the FASB issued Accounting Standards Update ("ASU") No. 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. This ASU is intended to define management's responsibility to evaluate whether there is substantial doubt about an organization's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and to provide related footnote disclosures even in circumstances where conditions are mitigated as a result of management's plans. This guidance is effective for fiscal years ending after December 15, 2016, with early application permitted. If this standard had been adopted as of June 30, 2016 and applied to these financial statements, the guidance would have required additional disclosure in the financial statements. The Company faces certain risks and uncertainties as further described in Note 1, "Organization," that may have an effect on the Company's disclosures in future periods.

In March 2016, the FASB issued ASU No. 2016-09, Compensation Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. This ASU is intended to simplify certain aspects of the accounting for share-based payment transactions, such as allowing entities to elect to account for forfeitures as they occur or to continue to estimate the number of awards that are expected to vest. The standard is effective for public entities for annual and interim periods beginning after December 15, 2016. The Company is currently evaluating the impact that the adoption of this standard will have on its financial statements.

(4) Collaborations and License Agreements

CANbridge

In March 2016, the Company entered into a collaboration and license agreement with CANbridge Life Sciences Ltd. ("CANbridge"). Under the terms of the license agreement, the Company granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, the Company's proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in humans and animals in all countries other than the United States,

Canada and Mexico (the “Licensed Territory”). Under the terms of the license agreement, if the Company determines to grant a license to any ErbB3 inhibitory antibody in the United States, Canada or Mexico, the Company is obligated to first negotiate with CANbridge for the grant to CANbridge of a license to such rights. In addition, for a period of time following the completion of certain proof-of-concept clinical studies by CANbridge involving the use of AV-203 for the treatment of squamous cell esophagus cancer, the Company has agreed to negotiate exclusively with CANbridge for (a) the right to co-develop ErbB3 inhibitory antibody products for the treatment of squamous cell esophagus cancer or (b) the right to include the United States, Canada and Mexico as part of the Licensed Territory under the license agreement. The effective date of the license agreement is March 16, 2016 (the “Effective Date”).

CANbridge made an upfront payment to the Company of $1.0 million in April 2016. This amount was included in accounts receivable on the Company’s balance sheet as of March 31, 2016 net of $0.1 million of withholding taxes. CANbridge has agreed to reimburse the Company $1.0 million for certain manufacturing costs and expenses previously incurred by the Company with respect to AV-203, $0.5 million of which will be due to the Company on the earlier of (i) the date of validation by CANbridge of certain manufacturing development activities conducted by the Company prior to the Effective Date or (ii) twelve months from the Effective Date, and the remaining $0.5 million of which will be due to the Company on the earlier of (i) the date of validation by CANbridge of such manufacturing development activities or (ii) eighteen months from the Effective Date. The Company is also eligible to receive up to $42.0 million in potential development and regulatory milestone payments and up to $90.0 million in potential sales based milestone payments based on annual net sales of licensed products. Upon commercialization, the Company is eligible to receive a tiered royalty, with a percentage range in the low double digits, on net sales of approved licensed products. CANbridge’s obligation to

pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity in such country and ten years after the first commercial sale of such licensed product in such country. No milestone payments have been earned as of June 30, 2016.

CANbridge is obligated to use commercially reasonable efforts to develop and commercialize AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain, and Germany. CANbridge has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of AV-203 in the Licensed Territory.

The term of the license agreement commenced on the Effective Date and will continue until the last to expire royalty term applicable to licensed products. Either party may terminate the license agreement in the event of a material breach by the other party that remains uncured for a period of 45 days, in the case of a material breach of a payment obligation, and 90 days in the case of any other material breach. CANbridge may terminate the license agreement without cause at any time upon 180 days' prior written notice to the Company. The Company may terminate the license agreement upon thirty days' prior written notice if CANbridge challenges any of the patent rights licensed to CANbridge under the license agreement.

The Company and CANbridge have each agreed to not directly or indirectly develop or commercialize any ErbB3 inhibitory antibody product during the term of the license agreement other than pursuant to the license agreement.

A percentage of any milestone and royalty payments received by the Company, excluding upfront and reimbursement payments, are due to Biogen Idec International GMBH ("Biogen") as a sublicensing fee under the option and license agreement between the Company and Biogen dated March 18, 2009, as amended.

Activities under the agreement were evaluated under ASC 605-25 Revenue Recognition—Multiple Element Arrangements, or ASC 605-25, to determine whether such activities represented a multiple element revenue arrangement. The agreement with CANbridge includes the following non-contingent deliverables: (i) the Company's grant of an exclusive license to develop and commercialize AV-203 in the licensed territories, (ii) the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of AV-203 and (iii) the Company's obligation to participate on a joint steering committee during the proof-of-concept development period. The relative selling price of the Company's joint steering committee participation had de minimis value. The Company determined that the delivered license and know-how did have stand-alone value from the undelivered element and have accounted for these items as separate deliverables. The Company allocated the up-front consideration of $1.0 million to the units of accounting and recognized the $1.0 million attributed to the delivered license and know-how during the three months ended March 31, 2016.

The Company believes the regulatory milestones that may be achieved under the license agreement are consistent with the definition of a milestone included in ASU 2010-17, Revenue Recognition—Milestone Method, and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when each such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

EUSA

In December 2015, the Company entered into a license agreement with EUSA Pharma (UK) Limited ("EUSA") 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, Australasia and New Zealand (the "Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye. EUSA filed an application with the

EMA in February 2016 for approval of marketing authorization for tivozanib for the treatment of RCC.

Under the license agreement, EUSA made a research and development funding payment to the Company of $2.5 million during the year ended December 31, 2015. EUSA is required to make a further research and development funding payment of $4.0 million upon the grant by the European Medicines Agency ("EMA") of marketing approval for tivozanib for treatment of RCC. The Company is eligible to receive additional research funding from EUSA, including up to $20.0 million for the Company's phase 3 study in third-line RCC if EUSA elects to utilize data generated by the study, and up to $2.0 million for a potential phase 1 combination study with a checkpoint inhibitor if EUSA elects to utilize data generated by the study. The Company will be entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for RCC in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. The Company is also eligible to receive a payment of $2.0 million in connection with EUSA's filing with the EMA for marketing approval for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as potentially up to $335.0 million upon EUSA's achievement of certain sales thresholds. The Company is also eligible to receive tiered double digit royalties on net sales, if any, of licensed products in the Licensed Territories ranging from a low double digit up to

mid-twenty percent depending on the level of annual net sales. A percentage of any milestone and royalty payments received by AVEO are due to Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.) ("KHK") as a sublicensing fee under the license agreement between AVEO and KHK dated as of December 21, 2006, pursuant to which the Company acquired exclusive rights to develop and commercialize tivozanib for all human diseases outside of Asia (the "KHK License Agreement"). The research and development funding payments under the EUSA license agreement are not subject to sublicensing payment to KHK.

EUSA is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the Licensed Territories. With the exception of certain support to be provided by the Company in connection with the application for marketing approval by the EMA, EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the Licensed Territories.

Activities under the agreement were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with EUSA includes the following non-contingent deliverables: (i) the Company's grant of an exclusive license to develop and commercialize the tivozanib in the licensed territories; (ii) the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of tivozanib; (iii) the Company's obligation to cooperate with EUSA and support its efforts to file for marketing approval in the licensed territories, (iv) the Company's obligation to provide access to certain regulatory information resulting from the Company's ongoing development activities outside of the licensed territories and (v) the Company's participation in a joint steering committee. The Company determined that the delivered license did not have stand-alone value from the undelivered elements and have accounted for these items as a single bundled deliverable. The Company allocated up-front consideration of $2.5 million to the bundled unit of accounting and is recognizing it over the Company's performance period through April 2022, the remaining patent life of tivozanib. The Company recognized approximately $0.1 million and $0.2 million as revenue during the three months and six months ended June 30, 2016, respectively.

The Company believes the regulatory milestones that may be achieved under the EUSA agreement are consistent with the definition of a milestone included in ASU 2010-17, Revenue Recognition—Milestone Method, and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when each such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone. No milestone payments have been earned as of June 30, 2016.

Novartis

In August 2015, the Company entered into a license agreement with Novartis. Under the license agreement, the Company has granted to Novartis the exclusive right to develop and commercialize worldwide the Company's proprietary antibody AV-380 and related AVEO antibodies that bind to Growth Differentiation Factor 15 ("GDF15") for the treatment and prevention of diseases and other conditions in all indications in humans (the "Product").

Pursuant to the license agreement, Novartis made an upfront payment to the Company of $15.0 million in September 2015. Novartis also has acquired the Company's inventory of clinical quality, AV-380 biological drug substance and reimbursed the Company for approximately $3.5 million for such existing inventory. The Company is also eligible to receive (a) up to $53.0 million in potential clinical and development milestone payments and up to $105.0 million in potential regulatory milestone payments tied to the commencement of clinical trials and to regulatory approvals of products developed under the license agreement in the United States, the European Union and Japan; and (b) up to $150.0 million in potential commercial milestone payments based on annual net sales of such products. Upon commercialization, the Company is eligible to receive tiered royalties on net sales of approved products ranging from the high single digits to the low double digits. Novartis has responsibility under the license agreement for the development, manufacture and commercialization of the Company's antibodies and any resulting approved therapeutic

products.

The Company has agreed that it will not directly or indirectly develop, manufacture or commercialize any GDF15 modulator as a human therapeutic during the term of the license agreement.

Activities under the agreement with Novartis were evaluated under ASC 605-25, to determine whether such activities represented a multiple element revenue arrangement. The agreement with Novartis includes the following non-contingent deliverables: (i) the Company's grant of an exclusive, worldwide license to develop and commercialize the Product; (ii) the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of the Product; and (iii) the Company's obligation to cooperate with Novartis' requests for transition assistance during a 90 day period. The Company determined that the option to purchase the Company's existing inventory was a contingent deliverable.

The Company determined the delivered license and obligation to transfer technical knowledge and data have standalone value from the undelivered cooperation. The Company allocated up-front consideration of $15.0 million to the delivered license and technical knowledge and recognized this amount as revenue during the year ended December 31, 2015. The relative selling price of the undelivered cooperation had de minimis value.

The Company received a cash payment of $3.5 million related to the delivery of its inventory of clinical quality drug substance to Novartis during the three months ended March 31, 2016. No amounts were due to the Company from Novartis as of June 30, 2016.

Pharmstandard

In August 2015, the Company entered into a license agreement with JSC "Pharmstandard-Ufimskiy Vitamin Plant," a company registered under the laws of the Russian Federation ("Pharmstandard"). Pharmstandard is a subsidiary of Pharmstandard OJSC. Under the license agreement, the Company has granted to Pharmstandard the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States (the "Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic ocular conditions.

In June 2016, following unsuccessful efforts to renegotiate certain terms of the Pharmstandard license agreement, Pharmstandard notified the Company that due to economic and market changes in Russia it was exercising its right to terminate the license agreement effective September 9, 2016. Upon termination of the license agreement, the licenses to tivozanib granted to Pharmstandard will terminate, all product rights and regulatory documents will be transferred to the Company, Pharmstandard will no longer be responsible for the development and commercialization of tivozanib in the Licensed Territories, and Pharmstandard will have no further payment obligations under the license agreement except with respect to payments that accrued prior to the effective date of the termination.

Pharmstandard filed an application for marketing authorization in Russia for tivozanib for the treatment of renal cell carcinoma that was accepted by the Ministry of Health of the Russian Federation in February 2016. The Company expects this application to be withdrawn following Pharmstandard's termination notice.

Activities under the agreement with Pharmstandard were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Pharmstandard includes the following non-contingent deliverables: (i) the Company's grant of an exclusive license to develop and commercialize tivozanib in the Licensed Territories, (ii) the Company's obligation to provide access, upon request, to all clinical data, regulatory filings, safety data and manufacturing data to Pharmstandard for use in the development and commercialization of tivozanib in the Licensed Territories, (iii) the Company's obligation to participate in certain development and commercialization planning meetings and (iv) the Company's obligation to provide support for certain development, regulatory or manufacturing activities if requested by Pharmstandard.

The Company determined the delivered license did not have standalone value from the undelivered items and that the arrangement should be treated as a single unit of accounting. The Company allocated the upfront payment of $1.0 million to the bundled unit of accounting and is recognizing it over the Company's performance period through April 2022, the remaining patent life of tivozanib. The Company recognized approximately $37,000 and $75,000 as revenue during the three months and six months ended June 30, 2016, respectively. Upon the effective date of the termination, the remaining deferred revenue of approximately $0.9 million will be recognized.

Ophthotech

In November 2014 the Company entered into a research and exclusive option agreement (the "Option Agreement"), with Ophthotech Corporation ("Ophthotech") pursuant to which the Company provided Ophthotech an exclusive option to enter into a definitive license agreement whereby the Company would grant Ophthotech the right to develop and commercialize tivozanib outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

Pursuant to this Option Agreement, the Company granted to Ophthotech an exclusive, royalty-free license or sublicense, as applicable, under intellectual property rights controlled by the Company solely to perform the research and development activities related to the use of tivozanib for the specific purposes outlined in the agreement during the Option Period (as defined below). These activities include formulation work for ocular administration, preclinical research and the conduct of a phase 1/2a, proof of concept clinical trial of a product containing tivozanib in patients with wet age-related macular degeneration, (the “POC Study”).

Ophthotech paid the Company $0.5 million in consideration for the grant of the option. Such amount is non-refundable and not creditable against any other amounts due under the agreement. The Company is obligated to make available to Ophthotech, at no cost to Ophthotech, certain quantities of tivozanib hydrochloride solely for conducting its Option Period research including manufacturing additional quantities of tivozanib in the event stability data indicates that the current supply will expire prior to the end of February 2017.

During the Option Period, if Ophthotech elects to continue the development of tivozanib for non-oncologic diseases of the eye, the Company is entitled to receive a one-time milestone payment of $2.0 million upon acceptance of the first Investigational New

Drug application for the purpose of conducting a human clinical study of tivozanib in ocular diseases (the "IND Submission Milestone Payment"). The Company is also entitled to receive a one-time milestone payment of $6.0 million (the "Clinical Efficacy Milestone Payment"), on the earlier of (a) December 31, 2016 and (b) the later to occur of: (i) the achievement of a clinical milestone in the POC Study (the "Clinical Efficacy Milestone") and (ii) the earlier of (A) the date twelve (12) months after our and Ophthotech's agreement as to the form and substance of the KHK Amendment (as defined below) or (B) the date ninety (90) days after the entry into the KHK Amendment, subject to Ophthotech's right to terminate the Option Agreement on 90 days' written notice and certain other conditions (the date on which such payment is due, referred to as the "Clinical Efficacy Milestone Payment Trigger Date").

Ophthotech may exercise the option at any time until the latest to occur of: (i) twelve (12) months after the achievement of the Clinical Efficacy Milestone, (ii) ninety (90) days after the Clinical Efficacy Milestone Payment Trigger Date, and (iii) thirty (30) days after the Company and Ophthotech agree as to the definitive form of license agreement (the "Option Period").

During the Option Period, the Company will not grant a license to any third party that would preclude the Company from being able to grant to Ophthotech the rights and licenses that are contemplated by the definitive license agreement, and the Company will not engage in any research, development or commercialization of tivozanib in the field covered by the contemplated definitive license agreement, except as specified in the Option Agreement.

The terms of the Option Agreement are subject to the Company's obligations to KHK under the KHK License Agreement. A percentage of all payments received by the Company under the Option Agreement and any definitive license agreement must be paid to KHK. The Company is required to maintain the KHK License Agreement in effect, and not enter into any amendment or termination thereof that would adversely affect the Company's rights, during the option period.

During the Option Period, the Company and Ophthotech are obligated to negotiate in good faith the form and substance of a definitive license agreement, as well as the form and substance of an amendment to the KHK License Agreement (the "KHK Amendment") to modify certain rights and obligations of the parties and sublicensees thereunder, particularly with respect to rights to improvements that are not specifically related to tivozanib, and regulatory affairs matters.

If Ophthotech exercises the option, Ophthotech is required to pay the Company a one-time option exercise fee of $2.0 million in addition to the IND Submission Milestone Payment if such payment has not then been previously paid. If upon exercise of the option, the Clinical Efficacy Milestone Payment Trigger Date has not yet occurred, the Company shall be entitled to the Clinical Efficacy Milestone Payment at such time that the Clinical Efficacy Milestone Payment Date does occur if the license agreement remains in effect as of such date. The license agreement, if entered into upon Ophthotech's exercise of the option, will provide for the Company to be entitled to receive (i) $10.0 million upon meeting certain efficacy and safety endpoints in phase 2 clinical trials that would enable the commencement of a phase 3 clinical trial, (ii) $20.0 million upon marketing approval in the United States, (iii) $20.0 million upon marketing approval in the UK, Germany, Spain, Italy and France and (iv) up to $45.0 million in sales-based milestone payments. Ophthotech would also be required to pay tiered, double digit royalties, up to the mid-teens, on net sales of tivozanib or products containing tivozanib.

Activities under the agreement with Ophthotech were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Ophthotech includes the following non-contingent deliverables: (i) the Company's obligation to grant an exclusive option to Ophthotech to enter into a license agreement to develop and commercialize products incorporating tivozanib for treatment of diseases of the eye outside of Asia during the Option Period (the "Option Grant Deliverable"); (ii) the Company's obligation to enter into an amendment with KHK to modify the terms of the existing KHK agreement to negotiate a mutually acceptable form of license agreement; and (iii) the Company's obligation to transfer research-grade tivozanib drug substance for Ophthotech to conduct the Option Period research.

The Company determined that the delivered Option Grant Deliverable did not have standalone value from the remaining deliverables since Ophthotech could not obtain the intended benefit of the option without the remaining deliverables. Similarly, the remaining deliverables have no standalone value without the Option Grant Deliverable. The Company is accounting for the deliverables as one unit of accounting.

Under the Option Agreement, the Company received a cash payment of $0.5 million during the year ended December 31, 2014. The Company deferred the payment and is recording the deferred revenue over the Company's period of performance, which is currently estimated to be through December 2017. The Company recorded approximately $29,000 of revenue in each of the three months ended June 30, 2016 and 2015, and approximately $58,000 of revenue in each of the six months ended June 30, 2016 and 2015.

Biodesix

In April 2014, the Company entered into a worldwide agreement with Biodesix to develop and commercialize ficlatuzumab, the Company's its hepatocyte growth factor ("HGF") inhibitory antibody, with BDX004, a proprietary companion diagnostic test developed by Biodesix and derived from VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced non-small cell lung cancer ("NSCLC"). Under the agreement, the Company granted Biodesix perpetual, non-exclusive rights to certain intellectual property, including all clinical and biomarker data related to ficlatuzumab, to develop and commercialize BDX004. Biodesix granted the Company perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to BDX004, with respect to the development and commercialization of ficlatuzumab; each license includes the right to sublicense, subject to certain exceptions. Pursuant to a joint development plan, the Company retains primary responsibility for clinical development of ficlatuzumab in a proof of concept ("POC") clinical study of ficlatuzumab for NSCLC, in which VeriStrat will be used to select clinical trial subjects, referred to as the NSCLC POC Trial. The NSCLC POC Trial will be fully funded by Biodesix up to a cap of $15.0 million. After the cap is reached, the Company and Biodesix will share all costs of the NSCLC trial equally. Under the Biodesix agreement all manufacturing costs are shared equally, and the Company and Biodesix will each be responsible for 50% of development and regulatory costs associated with all future clinical trials agreed-upon by Biodesix and the Company, including all milestone payments and royalties payable to third parties, if any.

Pending marketing approval of ficlatuzumab and subject to a commercialization agreement to be entered into after receipt of results from the NSCLC POC Trial, each party would share equally in commercialization profits and losses, subject to the Company's right to be the lead commercialization party.

Biodesix is solely responsible for the BDX004 development costs, as well as BDX004 sales and marketing costs. Subject to and following the approval of the BDX004 test as a companion diagnostic for ficlatuzumab, Biodesix has agreed to make the BDX004 test available and use commercially reasonable efforts to seek reimbursement in all geographies where ficlatuzumab is approved. The Company has agreed to reimburse Biodesix a pre-specified amount, under certain circumstances for BDX004 tests performed.

Prior to the first commercial sale of ficlatuzumab and after the earlier of (i) the Cap being reached or (ii) the completion of the NSCLC POC Trial, each party has the right to elect to discontinue participating in further development or commercialization efforts with respect to ficlatuzumab, which is referred to as an "Opt-Out". If either AVEO or Biodesix elects to Opt-Out, with such party referred to as the "Opting-Out Party", then the Opting-Out Party shall not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical trials. After election of an Opt-Out, the non-opting out party shall have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. Additionally, the Opting-Out Party shall be entitled to receive, if ficlatuzumab is successfully developed and commercialized, a royalty equal to 10% of net sales of ficlatuzumab throughout the world, if any, subject to offsets under certain circumstances.

If Biodesix elects to Opt-Out, it will continue to be responsible for its development and commercialization obligations with respect to BDX004. If AVEO elects to Opt-Out, it will continue to make the existing supply of ficlatuzumab available to Biodesix for the purposes of enabling Biodesix to complete the development of ficlatuzumab, and Biodesix will have the right to commercialize ficlatuzumab.

Prior to any Opt-Out, the parties shall share equally in any payments received from a third party licensee; provided, however, after any Opt-Out, the Opting-Out Party shall be entitled to receive only a reduced portion of such third party payments. The agreement will remain in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

Activities under the agreement with Biodesix were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Biodesix includes the following

non-contingent deliverables: (i) the Company's obligation to deliver perpetual, non-exclusive rights to certain intellectual property including clinical and biomarker data related to ficlatuzumab for use in developing and commercializing BDX004; (ii) the Company's obligation to deliver technology improvements and data developed during the NSCLC POC Trial to Biodesix; (iii) the Company's obligation to participate in the joint steering committee during the NSCLC POC Trial; (iv) the Company's obligation to perform certain development activities associated with the NSCLC POC Trial; (v) the Company's obligation to supply clinical material for use in conducting the NSCLC POC Trial; and (vi) the Company's obligation to deliver clinical specimens and data during the NSCLC POC Trial. The Company concluded that any deliverables that would be delivered after the NSCLC POC Trial is complete are contingent deliverables because these services are contingent upon the results of the NSCLC POC Trial. As these deliverables are contingent, and are not at an incremental discount, they are not evaluated as deliverables at the inception of the arrangement. These contingent deliverables will be evaluated and accounted for separately as each related contingency is resolved. As of June 30, 2016, no contingent deliverables had been provided by the Company.

The Company determined that the delivered item, or the perpetual, non-exclusive rights to certain intellectual property for use in developing and commercializing BDX004 did not have standalone value from the remaining deliverables since Biodesix could not

obtain the intended benefit of the license without the remaining deliverables. Since the remaining deliverables will be performed over the same period of performance there is no difference in accounting for the deliverables as one unit or multiple units of accounting, and therefore, the Company is accounting for the deliverables as one unit of accounting.

The Company records the consideration earned while conducting the NSCLC POC Trial, which consists of reimbursements from Biodesix for expenses related to the trial under the Cap, as a reduction to research and development expense using the proportional performance method over the respective period of performance. As a result of the cost sharing provisions in the agreement, the Company reduced research and development expenses by approximately $0.6 million and $1.5 million during the three months and six months ended June 30, 2016, respectively, and by approximately $1.0 million and $1.9 million during the three months and six months ended June 30, 2015, respectively. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was approximately $1.3 million at June 30, 2016, of which approximately $0.8 million was paid in July 2016. The Company received cash payments related to cost reimbursements of approximately $1.3 million and $1.8 million during the six months ended June 30, 2016 and 2015, respectively.

St. Vincent’s

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

In order to sublicense certain necessary intellectual property rights to Novartis in August 2015, the Company and St. Vincent’s amended and restated the license agreement (the “Amended St. Vincent’s Agreement”). Under the Amended St. Vincent’s Agreement, the Company was required to make an upfront payment to St. Vincent’s of $1.5 million. St. Vincent’s is also eligible to receive up to approximately $18.9 million in connection with development and regulatory milestones under the Amended St. Vincent’s Agreement. Royalties for approved products resulting from the Amended St. Vincent’s Agreement will also be payable to St. Vincent’s, and the Company and Novartis will share that obligation equally. Under the license agreement with Novartis, the Company is required to maintain the Amended St. Vincent’s Agreement in effect, and not enter into any amendment that would adversely affect Novartis’ rights during the term of the license agreement with Novartis.

During the six months ended June 30, 2016, the Company made a $0.4 million milestone payment to St. Vincent’s related to the selection of a development candidate.

Astellas Pharma

In February 2011, the Company, together with its wholly-owned subsidiary AVEO Pharma Limited, entered into a collaboration and license agreement (the “Astellas Agreement”) with Astellas Pharma Inc. and certain of its subsidiaries (together, “Astellas”), pursuant to which the Company and Astellas intended to develop and commercialize tivozanib for the treatment of a broad range of cancers. Astellas elected to terminate the agreement effective on August 11, 2014, at which time the tivozanib rights were returned to the Company. In accordance with the Astellas Agreement, committed development costs, including the costs of completing certain tivozanib clinical development activities, continue to be shared equally.

The Company accounted for the joint development and commercialization activities in North America and Europe as a joint risk-sharing collaboration in accordance with ASC 808, Collaborative Arrangements. Payments from Astellas

with respect to Astellas' share of tivozanib development and commercialization costs incurred by the Company pursuant to the joint development plan were recorded as a reduction to research and development expense and general and administrative expense in the accompanying consolidated financial statements due to the joint risk-sharing nature of the activities in North America and Europe. As a result of the cost-sharing provisions in the Astellas Agreement, the Company decreased research and development expenses by $0 and $0.4 million during the three months ended June 30, 2016 and 2015, respectively, and by $0.2 million in each of the six months ended June 30, 2016 and 2015. There is no outstanding balance due from Astellas pursuant to the cost-sharing provisions at June 30, 2016.

Under the agreement, the Company received cash payments related to reimbursable payments of $0.2 million and $34,000 during each of the three months ended June 30, 2016 and 2015, respectively, and $0.3 million and $0.6 million during the six months ended June 30, 2016 and 2015, respectively.

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, AV-203, for the potential treatment and diagnosis of cancer and other diseases outside of North America. Under the 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, will generate data sufficient to support advancement to a phase 3 clinical trial.

In March 2014, the Company and Biogen amended the exclusive option and license agreement (the "Amendment"). Pursuant to the Amendment, Biogen agreed to the termination of its rights and obligations under the agreement, including Biogen's option to (i) obtain a co-exclusive (with AVEO) 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, AVEO has worldwide rights to AV-203. Pursuant to the Amendment, the Company was obligated to use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The Company is also obligated to pay Biogen a percentage of milestone payments received by AVEO 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 cumulative maximum amount of $50 million.

The Company concluded that the Amendment materially modified the terms of the agreement and, as a result, required the application of ASC 605-25. Based upon the terms of the Amendment, the remaining deliverables included the Company's obligation to seek a collaboration partner to fund further development of the program and the Company's obligation to continue development and commercialization of the licensed products if a collaboration partner is secured ("Development Deliverable"). The Company concluded that its obligation to use best efforts to seek a collaboration partner does not have standalone value from the Development Deliverable upon delivery and thus the deliverables should be treated as a single unit of accounting.

Upon modifying the arrangement, the Company had $14.7 million of deferred revenue remaining to be amortized. The Company is not entitled to receive any further consideration from Biogen Idec under the amended arrangement. The Company allocated a portion of the remaining deferred revenue to the undelivered unit of accounting based upon the Company's best estimate of the selling price, as the Company determined that neither VSOE nor TPE were available. The Company determined the best estimate of selling price to be approximately $0.6 million and recognized the remaining $14.1 million as collaboration revenue in March 2014. The deferred revenue associated with the undelivered unit of accounting is being recognized on a straight-line basis over the period of performance, or through March 2016, when the Company executed its agreement with CANbridge.

Under the agreement, the Company recorded revenue of $0 and $38,000 during the three months and six months ended June 30, 2016, respectively, and $76,000 and $152,000 during the three months and six months ended June 30, 2015, respectively.

In March 2016, the Company entered into a collaboration and license agreement for AV-203 with CANbridge. See "Collaborations and License Agreements—CANbridge" herein for a further description of that arrangement.

(5) Other Accrued Liabilities

Other accrued expenses consisted of the following as of June 30, 2016 and December 31, 2015:

	June 30, 2016	December 31, 2015
	(in thousands)	
Professional fees	$592	$ 573
Compensation and benefits	552	938
Restructuring	51	357
Other	258	272
Total	$1,453	$ 2,140

(6) Loans Payable

On May 28, 2010, the Company entered into a loan and security agreement (the “Loan Agreement”) with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth (collectively, “Hercules”). The Loan Agreement was subsequently amended in March 2012, September 2014 (the “2014 Amendment”) and May 2016 (the “2016 Amendment”). Amounts borrowed under the March 2012 Amendment were repaid in full in 2015.

Pursuant to the 2014 Amendment, the Company received additional loan proceeds from Hercules in the amount of $10.0 million and was not required to commence principal payments until May 1, 2016, with the last principal payment due on January 1, 2018. An end-of-term payment of approximately $0.5 million continues to be due on January 1, 2018 or on such earlier date if the loan is prepaid. The Company incurred approximately $0.2 million in loan issuance costs paid directly to Hercules, which were offset against the loan proceeds and are accounted for as a loan discount. The 2014 Amendment was accounted for as a loan modification in accordance with ASC 470-50, Debt—Modifications and Extinguishments.

In connection with the 2014 Amendment, the Company issued warrants to the lenders to purchase up to 608,696 shares of the Company's common stock at an exercise price equal to $1.15 per share. The Company recorded the fair value of the warrants of approximately $0.4 million as stockholders' equity and as a discount to the related loan outstanding and is amortizing the value of the discount to interest expense over the term of the loan using the effective interest method.

Pursuant to the 2016 Amendment, the Company received additional loan proceeds from Hercules in the amount of $5.0 million, which increased the aggregate outstanding principal balance under the Loan Agreement to $15.0 million. The Company is not required to commence principal payments on the $15 million loan until July 1, 2017, at which time the Company will be required to make 30 equal monthly payments of principal and interest through December 2019. An end-of-term payment of approximately $0.2 million is due on December 1, 2019. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which were offset against the loan proceeds and are accounted for as a loan discount. The 2016 Amendment was accounted for as a loan modification in accordance with ASC 470-50, Debt—Modifications and Extinguishments. The 2016 Amendment includes a financial covenant that requires the Company to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of the Company's Phase 3 TIVO-3 trial.

Under the 2016 Amendment, the Company may, at its request during any time from March 1, 2017 through June 30, 2017, draw down an additional $5.0 million in funding. This funding is contingent upon the Company: (i) achieving satisfactory developmental progression on a minimum of two (2) clinical programs (other than the Phase 3 TIVO-3 trial) that are either managed directly by the Company or funded, in whole or in part, by the Company and (ii) having an unrestricted cash position greater than or equal to $25.0 million on the date of the draw down request. If the Company draws down the additional $5.0 million in funding, the commencement of principal payments on the aggregate $20.0 million loan balance will be deferred by six months from July 1, 2017 until January 1, 2018.

In connection with the 2016 Amendment, the Company issued warrants to Hercules to purchase up to 1,202,117 shares of the Company's common stock at an exercise price equal to $0.87 per share. The Company recorded the fair value of the warrants of approximately $0.7 million as stockholders' equity and as a discount to the related loan outstanding and is amortizing the value of the discount to interest expense over the term of the loan using the effective interest method.

The unamortized discount to be recognized over the remainder of the loan period was approximately $1.3 million and $0.5 million as of June 30, 2016 and December 31, 2015, respectively.

The Company must make interest payments on the loan balance each month it remains outstanding. Per annum interest is payable on the principal balance of the loan each month it remains outstanding at the greater of 11.9% and an amount equal to 11.9% plus the prime rate minus 4.75% as determined daily, provided however, that the per annum interest rate shall not exceed 15.0% (11.9% as of June 30, 2016).

As part of the Loan Agreement, Hercules also received an option, subject to the Company's written consent, not to be unreasonably withheld, to purchase, either with cash or through conversion of outstanding principal under the loan, up

to $2.0 million of equity of the Company sold in any sale by the Company to third parties of equity securities resulting in at least $10.0 million in net cash proceeds to the Company, subject to certain exceptions. The Company has evaluated the embedded conversion option, and has concluded that it does not need to be bifurcated and separately accounted for. No amount will be recognized for the conversion feature until such time as the conversion feature is exercised and it can be determined whether a beneficial conversion feature exists. In connection with the Company's May 2016 private placement (refer to Note 7), Hercules purchased 259,067 units for cash proceeds of $0.2 million to the Company. This purchase was separate from the $2.0 million equity purchase option under the Loan Agreement.

The loans are secured by a lien on all the Company's personal property (other than intellectual property), whether owned or acquired after the date of the Loan Agreement. The Loan Agreement defines events of default, including the occurrence of an event that results in a material adverse effect upon the Company's business operations, properties, assets or condition (financial or otherwise), its ability to perform its obligations or upon the ability of the lenders to enforce any of their rights or remedies with respect to such obligations, or upon the collateral under the Loan Agreement, the related liens or the priority thereof. As of June 30, 2016, 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 change 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 in current and long-term liabilities based on the timing of scheduled principal payments.

Future minimum payments under the loans payable outstanding as of June 30, 2016 are as follows (amounts in thousands):

Years Ending December 31:	
2016 (6 months remaining)	$907
2017	4,386
2018	7,507
2019	7,159
	19,959
Less amount representing interest	(4,268)
Less discount	(1,266)
Less deferred charges	(690)
Less current portion	—
Loans payable, net of current portion and discount	$13,735

(7) Common Stock

Private Placement / PIPE Warrants

In May 2016, the Company entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which the Company sold 17,642,482 units, at a price of $0.965 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of the Company's common stock and a warrant to purchase one share of the Company's common stock (the "PIPE Warrants"). The PIPE Warrants have an exercise price of $1.00 per share and are exercisable for a period of five years from the date of issuance. Certain of the Company's directors and executive officers purchased an aggregate of 544,039 units in this offering at the same price as the other investors. The net offering proceeds to the Company were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by the

Company.

The PIPE Warrants contain a provision giving the warrant holder the option to receive cash, equal to the fair value of the remaining unexercised portion of the warrant, as cash settlement in the event that there is a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, Distinguishing Liabilities from Equity requires that these warrants be classified as a liability and not as equity. Accordingly, the Company recorded a warrant liability in the amount of approximately $9.3 million upon issuance of the PIPE Warrants. The fair value of these warrants has been determined using the Black Scholes valuation model, and the changes in the fair value at the time of each reporting date are recorded in the Statements of Operations and Comprehensive Income (Loss). During the three months ended June 30, 2016, as a result of the fair value adjustment of the warrant liability, the Company recorded a non-cash loss on the increase in the fair value of approximately $1.0 million in the Statements of Operations and Comprehensive Income (Loss). As of June 30, 2016, none of the PIPE Warrants have been exercised.

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

	Original Issuance	June 30, 2016
Expected price volatility	76.25%	75.61%
Expected term (in years)	5.00	5.00
Risk-free interest rates	1.22%	1.01%
Dividend yield	—	—

ATM Sales Agreement

In February 2015, the Company entered into an at-the-market issuance sales agreement (the "Sales Agreement") with FBR & Co. (formerly MLV & Co. LLC) ("FBR"), pursuant to which the Company could issue and sell shares of its common stock from time to time up to an aggregate amount of $17.9 million, at the Company's option, through FBR as its sales agent. Sales of common stock through FBR may be 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, including by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by the Company and FBR. Subject to the terms and conditions of the Sales Agreement, FBR will use commercially reasonable efforts to sell the common stock based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company is not obligated to make any sales of its common stock under the Sales Agreement. Any shares sold will be sold pursuant to an effective shelf registration statement on Form S-3. The Company will pay FBR a commission of up to 3% of the gross proceeds. The Sales Agreement may be terminated by the Company at any time.

On May 7, 2015, the Company filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by the Company of up to $100.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "2015 Shelf"). The 2015 Shelf was filed to replace the Company's existing $250.0 million shelf registration statement (the "2012 Shelf"). On May 7, 2015, the Company also amended its Sales Agreement with FBR to provide for the offering, issuance and sale by the Company of up to $15.0 million of its common stock under the 2015 Shelf, which replaced the Company's existing $17.9 million offering that expired along with the expired 2012 Shelf. As of June 30, 2016, the Company has sold approximately 5.9 million shares pursuant to the Sales Agreement, as amended, resulting in proceeds of approximately $10.2 million, net of commissions and issuance costs. No shares have been sold during the three and six months ended June 30, 2016.

Approximately $9.1 million remains available for sale under the Sales Agreement.

(8) Stock-based Compensation

Stock Plans

The following table summarizes stock option activity during the six months ended June 30, 2016.

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2015	4,796,005	$ 3.78		

Granted	1,644,934	$ 1.03		
Exercised	(35,416)	$ 0.84		
Forfeited	(577,252)	$ 1.82		
Outstanding at June 30, 2016	5,828,271	$ 3.22	7.27	$ 142
Vested or expected to vest at June 30, 2016	3,910,379	$ 4.23	6.37	$ 94
Exercisable at June 30, 2016	2,752,710	$ 5.55	5.31	$ 45

Stock options to purchase 200,665 shares of common stock contain market conditions which were not deemed probable of vesting at June 30, 2016.

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

	Three Months Ended	
	June 30,	
	2016	2015
Volatility factor	73.2% - 74.4%	74.0% - 77.6%
Expected term (in years)	5.50 - 6.25	5.50 - 6.25
Risk-free interest rates	0.94% - 1.03%	1.78% - 1.85%
Dividend yield	—	—

	Six Months Ended June 30,	
	2016	2015
Volatility factor	73.24% - 74.47%	73.04% - 78.7%
Expected term (in years)	5.50 - 6.25	5.50 - 6.25
Risk-free interest rates	0.94% - 1.38%	1.54% - 1.85%
Dividend yield	—	—

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

The Company does not have sufficient history to support a calculation of volatility and expected term using only its historical data. As such, the Company has used a weighted-average volatility considering the Company's own volatility since March 2010, and the volatilities of several peer companies. For purposes of identifying similar entities, the Company considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. Due to lack of available option activity data, the Company elected to use the "simplified" method for "plain vanilla" options to estimate the expected term of the 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. Based upon these assumptions, the weighted-average grant date fair value of stock options granted to employees during the six months ended June 30, 2016 and 2015 was $1.03 per share and $1.13 per share, respectively.

The Company is required to include an estimate of the value of the awards that will be forfeited in calculating compensation costs, which the Company estimates based upon actual historical forfeitures. The forfeiture estimates are recognized over the requisite service period of the awards on a straight-line basis. The Company estimated its forfeiture rate to be approximately 76% and 71% as of June 30, 2016 and 2015, respectively.

As of June 30, 2016, there was $0.8 million of total unrecognized stock-based compensation expense related to stock options granted to employees under the Company's 2002 Stock Incentive Plan and 2010 Stock Incentive Plan (collectively, the "Plans"). The expense is expected to be recognized over a weighted-average period of 2.8 years. The intrinsic value of options exercised during the three and six months ended June 30, 2016 was $35,000 and $35,000, respectively. The intrinsic value of options exercised during the three and six months ended June 30, 2015 was $44,000 and $57,000, respectively.

The restricted stock activity for the six months ended June 30, 2016 is as follows:

	Number of Shares	Weighted-Average

		Fair-Value
Unvested at December 31, 2015	42,750	$ 1.61
Granted	—	—
Vested/Released	(42,750)	1.61
Unvested at June 30, 2016	—	—

As of June 30, 2016, there was no unrecognized stock-based compensation expense related to restricted stock awards granted under the Plan.

(9) Strategic Restructuring

On January 6, 2015, the Board of the Company approved a strategic restructuring of the Company that eliminated the Company's internal research function and aligned the Company's resources with the Company's future strategic plans. As part of this restructuring, the Company eliminated approximately two-thirds of the Company's workforce, or 40 positions across the organization. The Company substantially completed the restructuring during the quarter-ended March 31, 2015.

The following table summarizes the components of the Company's restructuring activity recorded in operating expenses and in accrued expenses in the accompanying consolidated balance sheet:

	Restructuring amounts accrued at December 31, 2015	Restructuring expense incurred during the six months ended June 30, 2016	Restructuring amounts paid during the six months ended June 30, 2016	Restructuring amounts accrued at June 30, 2016
	(in thousands)			
Employee severance, benefits and related costs.	$357	—	$ (306)	51

The Company is obligated to continue to pay the remaining amounts accrued through the third quarter of 2016.

(10) Facility Lease Exit

In September 2014, the Company entered into the Lease Termination Agreement pursuant to which the Company immediately surrendered leased space at 650 East Kendall Street in Cambridge, Massachusetts that it had previously ceased using earlier in 2014. In connection with the Lease Termination Agreement, the Company agreed to pay the landlord a termination fee totaling $15.6 million. The Company also agreed to surrender its remaining leased space upon 90 days written notice prior to September 24, 2015.

In February 2015, the Company provided notice that it would surrender the remaining space on May 29, 2015. Accordingly, the Company revised the estimated useful life of its leasehold improvements related to this office space and amortized such assets through May 2015, resulting in an additional $2.9 million of depreciation expense during the six months ended June 30, 2015. Similarly, the Company accelerated the amortization of its deferred rent and leasehold improvement allowance associated with this office space through May 2015, resulting in an additional $3.5 million of amortization during the six months ended June 30, 2015. Upon the surrender of the remaining space, the Company had no further rights or obligations with respect to the lease. The Company secured office space appropriate for its current needs under a cancellable arrangement that began in May 2015.

(11) Legal Proceedings

Two class action lawsuits have been filed against the Company and certain of its former officers and members of its board of directors, (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer and Ronald DePinho), in the United States District Court for the District of Massachusetts, one captioned Paul Sanders v. Aveo Pharmaceuticals, Inc., et al., No. 1:13-cv-11157-JLT, filed on May 9, 2013, and the other captioned Christine Krause v. AVEO Pharmaceuticals, Inc., et al., No. 1:13-cv-11320-JLT, filed on May 31, 2013. On December 4, 2013, the District Court consolidated the complaints as In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC, and an amended complaint was filed on February 3, 2014. The amended complaint purported to be brought on behalf of shareholders who purchased the Company's common stock between January 3, 2012 and May 1, 2013. The amended complaint generally alleged that the Company and certain of its present and former officers and directors violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the phase 3 trial design and results for the Company's TIVO-1 study in an effort to lead investors to believe that the drug would receive approval from the FDA. The lawsuit seeks unspecified damages, interest, attorneys' fees, and other costs. The consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations. The Company moved to dismiss again, and after a second round of briefing and oral argument, the court ruled in the Company's favor and dismissed the second amended complaint with prejudice on November 18, 2015. The lead plaintiffs have appealed the court's decision to the United States Court of Appeals for the First Circuit. They have also filed a motion to vacate and reconsider the district court's judgment, which we have opposed. The Company denies any allegations of wrongdoing and intends to continue to vigorously defend against this lawsuit. However, there is no assurance that the Company will be successful in its defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of the action. Moreover, the Company is unable to predict the outcome or reasonably estimate a range of possible loss at this time.

On April 4, 2014, Karen J. van Ingen, a purported purchaser of AVEO stock, filed a derivative complaint allegedly on behalf of AVEO in the United States District Court for the District of Massachusetts, Civil Action No. 1:14-cv-11672-DJC, naming AVEO, as a nominal defendant and also naming as defendants present and former members of the Company's board of directors, including Tuan Ha-Ngoc, Henri A. Termeer, Kenneth M. Bate, Anthony B. Evnin, Robert Epstein, Raju Kucherlapati, Robert C. Young, and Kenneth E. Weg. The complaint alleged breach of fiduciary duty and abuse of control between January 2012 and May 2013 with respect to allegedly misleading statements and omissions regarding tivozanib. The lawsuit seeks, among other relief, unspecified damages, costs and expenses, including attorneys' fees, an order requiring us to implement certain corporate governance reforms, restitution from the

defendants and such other relief as the court might find just and proper. The Company filed a motion to dismiss the derivative complaint, and after briefing and oral argument, on March 18, 2015 the Court ruled in the Company's favor and dismissed the case with prejudice. The plaintiff then filed a motion seeking to vacate the Court's order of dismissal and permit filing of an amended complaint, which the Company opposed, and which the Court denied on June 30, 2015. The plaintiff has appealed the Court's decision to the United States Court of Appeals for the First Circuit. The parties have reached an agreement in principle to settle this matter. The settlement involves certain corporate governance changes and other non-monetary relief. The plaintiffs will seek an award of attorney's fees, which the Company expects will be paid by insurance. The settlement is subject to negotiation of final documentation and court approval. There can be no assurance that the settlement will be approved by the court.

On July 3, 2013, the staff (the "SEC Staff") of the United States Securities and Exchange Commission (the "Commission") served a subpoena on the Company for documents and information concerning tivozanib, including related communications with the FDA, investors and others. In September 2015, the SEC Staff invited the Company to discuss the settlement of potential claims asserting that the Company violated federal securities laws by omitting to disclose to investors the recommendation made to the Company by the staff of the FDA on May 11, 2012, that the Company conduct an additional clinical trial with respect to tivozanib. The Company agreed to settle those claims for a total amount of $4.0 million, subject to the approval of the Commission.

On March 29, 2016, the Commission filed a complaint against the Company and three of its former officers in the U.S. District Court for the District of Massachusetts (the "Court") alleging that the Company misled investors about its efforts to obtain FDA approval for tivozanib. Without admitting or denying the allegations in the Commission's complaint, the Company consented to the entry of a final judgment pursuant to which the Company paid the Commission a $4 million civil penalty to settle the Commission's claims against the Company. On March 31, 2016, the Court entered a final judgment which (i) approved the settlement; (ii) permanently enjoined the Company from violating Section 17(a) of the Securities Act of 1933, as amended, Sections 10(b) and 13(a) of the Securities Exchange Act of 1934, as amended, and rules 10b-5, 12b-20, 13a-1, 13a-11 and 13a-13 promulgated thereunder; and (iii) ordered the Company to pay the agreed-to civil penalty. The Commission's action against the Company's three former officers is still pending. The Company is not a party to any litigation or discussions between the SEC Staff and the former officers, and the Company can make no assurance regarding the outcome of that action or the Commission's claims against those individuals.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Forward-Looking Information

This report contains forward-looking statements regarding, among other things, our future development efforts, our collaborations, our future operating results and financial position, our business strategy, our prospects and other objectives for our operations. You can identify these forward-looking statements by their use of words such as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "plan," "project," "target," "will" and other words and terms meaning. You also can identify them by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our clinical development activities, our ability to obtain any necessary financing to conduct our planned activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our dependence on our existing and future strategic partners, and other risk factors. Please refer to the section entitled "Risk Factors" in Item 1A of Part II and elsewhere in this report for a description of these risks and uncertainties. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

Company Overview

We are a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. Our proprietary platform has delivered unique insights into cancer and related diseases. Our strategy is to leverage these biomarker insights and partner resources to advance the development of our clinical pipeline. We are focused on developing our lead candidate tivozanib in North America as a treatment for renal cell carcinoma. We have entered into partnerships to fund the further development of our clinical stage assets, including AV-380, ficlatuzumab, AV-203, and tivozanib in non-oncologic indications worldwide and oncology indications outside North America. We are currently seeking a partner to develop AV-353, a preclinical asset, worldwide in pulmonary arterial hypertension, or PAH.

Tivozanib

Tivozanib is a potent, selective, long half-life vascular endothelial growth factor (VEGF) tyrosine kinase inhibitor (TKI) of VEGF receptors 1, 2 and 3. In 2006, we acquired the exclusive rights to develop and commercialize tivozanib in all countries outside of Asia under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co. Ltd.), or KHK.

Clinical and Regulatory Development in RCC

RCC First Line Phase 3 Trial (TIVO-1): We conducted a global phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy, for first-line treatment of renal cell carcinoma, or RCC, which we refer to as the TIVO-1 trial. The trial met its primary endpoint for progression-free survival, or PFS, but showed a non-statistically significant trend favoring the sorafenib arm in overall survival, or OS. In June 2013, the U.S. Food and Drug Administration, or FDA, issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of advanced RCC based on the study data from this trial, and recommended that we perform an additional study adequately sized to assure the FDA that there is no adverse effect on OS.

In January 2015, we announced our receipt of confirmation from the European Medicines Agency, or EMA, that tivozanib is eligible for submission of an application for a European Union Marketing Authorization under the EMA's centralized procedure for the treatment of RCC. Confirmation of eligibility for submission is not predictive of the

EMA's approval of a Marketing Authorization Application, or MAA. Tivozanib has previously been granted orphan drug designation in Europe for the treatment of RCC. Our partner, EUSA Pharma (UK) Limited, or EUSA, submitted a MAA for tivozanib for the treatment of RCC with the EMA in February 2016 based on our existing dataset, which includes the results from the TIVO-1 study of tivozanib in the first-line treatment of RCC. In March 2016, the EMA validated the MAA, confirming that the submission was complete and that it would initiate its review process. EUSA received the Day 120 List of Questions from the EMA on July 21, 2016.

In December 2015, our partner JSC "Pharmstandard-Ufimskiy Vitamin Plant", a subsidiary of Pharmstandard OJSC, or Pharmstandard, submitted an application for marketing authorization for tivozanib based on the TIVO-1 trial results in Russia that was accepted for review by the Russian Ministry of Health in February 2016. We expect this application to be withdrawn following Pharmstandard's election to terminate our partnership, which is discussed further below under "-Strategic Partnerships -Pharmstandard Group".

TIVO-1 Extension Study - One-way crossover from sorafenib to tivozanib (Study 902): We completed a TIVO-1 extension study in which patients with advanced RCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib arm in the TIVO-1 first-line RCC trial. We presented the final results at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2015. The final results showed a median PFS of 11.0 months and a median OS of 21.6 months,

demonstrating the clinically meaningful efficacy of tivozanib in a VEGF treatment refractory population. We believe that the long OS derived from tivozanib following sorafenib in Study 902 contributed to the discordance in the results in the TIVO-1 trial between the PFS benefit, which significantly favored tivozanib, and the OS, which trended in favor of sorafenib. The FDA did not accept this explanation, finding that the OS results were confounded by the one-way crossover, and recommended that we perform a second phase 3 trial.

RCC Third Line Phase 3 Trial (TIVO-3): In May 2016, we initiated enrollment and treatment of patients in our new phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC. The TIVO-3 trial was designed to address the OS concerns from the TIVO-1 trial presented in the June 2013 complete response letter from the FDA and to support a request for regulatory approval of tivozanib in the United States as a third-line treatment and as a first-line treatment. Our study design, which we reviewed with the FDA, provides for a randomized, controlled, multi-center, open-label phase 3 study of approximately 322 subjects randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the study may include those who have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting a potentially evolving treatment landscape. The primary objective of the study is to show improved PFS, and secondary endpoints include OS and objective response rate, or ORR, as well as safety and pharmacokinetic endpoints. The study's sites are located in North America and the European Union. The study does not include a crossover. Following the initiation of enrollment, we continue to expect to report top line data from the study in the first quarter of 2018.

RCC PD-1 Combination Trial: We are planning to conduct a phase 1/2 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC. In recent studies, TKIs and PD-1 inhibitors have shown promising efficacy in treating RCC in combination. However, several TKI/PD-1 combinations have encountered toxicity levels that are likely to prohibit such TKIs from safely combining with PD-1 inhibitors for RCC treatment. In our clinical trials, tivozanib has demonstrated a superior tolerability profile relative to many other TKIs, including lower rates of key potential overlapping toxicities with PD-1 inhibitors. We believe that tivozanib's tolerability profile has the potential to allow tivozanib to combine with PD-1 inhibitors more safely than other TKIs.

Tivozanib Partnerships

EUSA License Agreement: In December 2015, we entered into a license agreement with EUSA Pharma (UK) Limited, or EUSA, under which we granted EUSA the right to develop and commercialize tivozanib for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye, in Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand.

Pharmstandard License Agreement: In August 2015, we entered into a license agreement under which we granted to Pharmstandard the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States, or CIS, for all conditions excluding non-oncologic ocular conditions. In June 2016, following unsuccessful efforts to renegotiate certain terms of the Pharmstandard license agreement, Pharmstandard notified us that due to economic and market changes in Russia it was terminating the license agreement. We plan to seek a new partner for the development and commercialization of tivozanib in these territories.

Ophthotech Option for Ocular Conditions (Non-Oncologic): In November 2014, we entered into a research and exclusive option agreement with Ophthotech Corporation, or Ophthotech, under which we granted Ophthotech a limited research license and an option for a license to develop and commercialize tivozanib outside of Asia for the diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

CRC Development

CRC Phase 2 Results: In March 2015, we announced results from a predefined biomarker analysis of our BATON-CRC study, as recently published in Clinical Cancer Research (Benson et. al., Clin. Ca. Res., ePub ahead of Print July 2016). The BATON-CRC study was a randomized phase 2 clinical trial of modified FOLFOX6, a commonly used chemotherapy, combined with tivozanib or Avastin® (bevacizumab), which both target angiogenesis signaling pathways, in first-line treatment of metastatic CRC. In this study, among prospectively defined biomarkers, patients with low (below the median, representing 50% of the population) serum neuropilin-1, or NRP-1, demonstrated longer PFS when treated with tivozanib compared to bevacizumab, which suggests that first-line colorectal cancer patients with low NRP-1 levels may benefit from treatment with tivozanib over bevacizumab, a standard of care in this disease. However, the assay used to measure serum NRP-1 is not suitable for development as a companion diagnostic. We do not plan to conduct further clinical studies unless an assay is identified.

Ficlatuzumab

Ficlatuzumab is a potent Hepatocyte Growth Factor, or HGF, inhibitory antibody. HGF is the sole known ligand of the c-Met receptor which is believed to trigger many activities that are involved in cancer development and metastasis. We have completed two phase 1 clinical studies of ficlatuzumab administered as a single agent and in combination with erlotinib (an EGFR TKI) and a phase 2 clinical study evaluating ficlatuzumab in combination with gefitinib (an EGFR TKI), in first-line non-small cell lung cancer, or NSCLC. The phase 2 trial failed to demonstrate a statistically significant benefit in the intent-to-treat population. However, an exploratory analysis using a serum-based proteomic diagnostic test, known as VeriStrat®, identified a sub-population of patients who experienced progression free survival and overall survival benefits from the addition of ficlatuzumab to gefitinib. VeriStrat is

commercially available to help physicians guide treatment decisions for patients with second-line advanced NSCLC. Data from the exploratory analyses with VeriStrat prompted the development of a separate investigational companion diagnostic test called BDX004. Based upon the exploratory analyses, we believe that BDX004 may be indicative of a predictive biomarker for the combination of ficlatuzumab and an EGFR TKI over an EGFR TKI alone in first-line EGFR mutation patients who have been previously identified to not respond well to the current standard of care.

In April 2014, we entered into a worldwide agreement with Biodesix, Inc., or Biodesix, to develop and commercialize ficlatuzumab with BDX004. Pursuant to the Biodesix agreement, in December 2014 we initiated a phase 2 confirmatory study, which we refer to as the FOCAL study, of ficlatuzumab in combination with erlotinib in first-line advanced NSCLC patients who have an EGFR mutation and who are identified by the BDX004 test as being most likely to benefit from the addition of ficlatuzumab to the EGFR TKI. We began enrolling patients during the second half of 2015. To date, enrollment has been slow due to a variety of factors. Under the Biodesix agreement, Biodesix agreed to fund up to $15 million of the costs of this study, after which costs are to be shared equally. Any additional development, regulatory and commercial costs under the Biodesix agreement are to be shared equally. Under the Biodesix agreement, subject to regulatory approval, we would lead worldwide commercialization of ficlatuzumab.

AV-203

AV-203 is a potent anti-ErbB3 (also known as HER3) specific monoclonal antibody with high ErbB3 affinity. We have observed potent anti-tumor activity in mouse models. AV-203 selectively inhibits the activity of the ErbB3 receptor, and our preclinical studies suggest that neuregulin-1, or NRG1 (also known as heregulin), levels predict AV-203 anti-tumor activity. We have completed a phase 1 dose escalation study of AV-203, which established a recommended phase 2 dose, demonstrated good tolerability and promising early signs of activity, and reached the maximum planned dose of AV-203 monotherapy. In 2014, for business reasons, the expansion cohort of this study was discontinued.

In March 2016, we entered into collaboration and license agreement with CANbridge Life Sciences Ltd., or CANbridge, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203 in all countries other than the United States, Canada and Mexico.

AV-380

AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment or prevention of cachexia. Cachexia is defined as a multi-factorial syndrome of involuntary weight loss characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. Cachexia is associated with various cancers as well as chronic kidney disease, congestive heart failure, and chronic obstructive pulmonary disease, or COPD. We believe that AV-380 represents a unique approach to treating cachexia because it addresses key underlying mechanisms of the syndrome. AV-380 focuses on a significant area of patient need. It is estimated that approximately 30% of all cancer patients die due to cachexia and over half of cancer patients who die do so with cachexia present (J Cachexia Sarcopenia Muscle 2010). In the United States alone, the estimated prevalence of cancer cachexia is over 400,000 patients, and the prevalence of cachexia due to cancer, COPD, congestive heart failure, frailty and end stage renal disease combined is estimated to total more than 5 million patients (Am J Clin Nutr 2006).

We have demonstrated preclinical proof-of-concept for AV-380 in multiple cancer cachexia models and have completed cell line development. In September 2014, we presented the results from four preclinical studies of AV-380 in various in vivo cachexia models and in vitro assays at the 2nd Cancer Cachexia Conference in Montreal Canada. Our research was also selected for presentation in an oral session at the conference. In April 2015, we also presented the results from a preclinical study of AV-380 in a cachectic human tumor xenograft model at the Annual Meeting of the American Association of Cancer Research. We have established preclinical proof of concept for

GDF15 as a key driver of cachexia by demonstrating, in animal models, that the administration of GDF15 induces cachexia, and that inhibition of GDF15 reverses cachexia and provides a potential indication of an overall survival benefit.

In August 2015, we entered into a license agreement under which we granted Novartis International Pharmaceutical Ltd., or Novartis, the exclusive right to develop and commercialize AV-380 and our related antibodies. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide. In connection with the AV-380 program, we have in-licensed certain patents and patent applications from St. Vincent's Hospital in Sydney, Australia.

AV-353

AV-353 is a potent inhibitory antibody specific to Notch 3. The Notch 3 signaling pathway is important in cell-to-cell communication involving gene regulation mechanisms that control multiple cell differentiation processes during the entire life cycle. Scientific literature has implicated the Notch 3 receptor pathway in multiple diseases, including cancer, cardiovascular diseases and

neurodegenerative conditions. Publications, including Nature Medicine (2009), have implicated the Notch 3 pathway in PAH, a rare and life-threatening disorder that affects approximately 250,000 people worldwide and is caused by enlargement of the arterial walls in small arteries between the heart and the lungs, resulting in restricted blood flow. Currently, no known cure for PAH exists. Existing treatments in PAH have focused on controlling symptoms by avoiding vasoconstriction and increasing vasodilation of blood vessels and have not reversed the underlying cause of the disease. In contrast, with the results of a recently concluded research study supported by the Company, AV-353 has generated a growing body of preclinical data that supports AV-353's ability to potentially reverse the disease phenotype, which would represent a potential disease-modifying approach to treatment. A manuscript of the results is being prepared for submission to a peer-reviewed journal.

We own worldwide rights to AV-353, which was developed utilizing our research and development platform and for which we have filed three composition of matter patent applications. We are currently seeking a partner to develop AV-353 worldwide in PAH.

Strategic Partnerships

CANbridge

On March 16, 2016, which we refer to as the Effective Date, we entered into a collaboration and license agreement with CANbridge under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, our proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in humans and animals in all countries other than the United States, Canada and Mexico. Under the terms of the license agreement, if we determine to grant a license to any ErbB3 inhibitory antibody in the United States, Canada or Mexico, we are obligated to first negotiate with CANbridge for the grant to CANbridge of a license to such rights. In addition, for a period of time following the completion of certain proof-of-concept clinical studies by CANbridge involving the use of AV-203 for the treatment of squamous cell esophagus cancer, we have agreed to negotiate exclusively with CANbridge for (a) the right to co-develop ErbB3 inhibitory antibody products for the treatment of squamous cell esophagus cancer or (b) the right to include the United States, Canada and Mexico as part of the licensed territory under the license agreement. The parties have both agreed not to directly or indirectly develop or commercialize any ErbB3 inhibitory antibody product during the term of the license agreement other than pursuant to the license agreement.

CANbridge is obligated to use commercially reasonable efforts to develop and commercialize AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain, and Germany. CANbridge has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of AV-203 in the licensed territory.

Pursuant to the license agreement, CANbridge paid us an upfront fee of $1.0 million in April 2016. CANbridge also agreed to reimburse us $1.0 million for certain manufacturing costs and expenses that we previously incurred, $0.5 million of which will be due on the earlier of (i) the date of validation by CANbridge of certain manufacturing development activities we conducted and (ii) twelve months from the Effective Date, and the remaining $0.5 million of which will be due on the earlier of (i) the date of validation by CANbridge of such manufacturing development activities or (ii) eighteen months from the Effective Date. We are also eligible to receive up to $42.0 million in potential development and regulatory milestone payments and up to $90.0 million in potential sales based milestone payments based on annual net sales of licensed products. Upon commercialization, we are eligible to receive a tiered royalty, with a percentage range in the low double digits, on net sales of approved licensed products. CANbridge's obligation to pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity in such country and ten years after the first commercial sale of such licensed product in such country. A percentage of any milestone and royalty payments received by us, excluding upfront and reimbursement payments, are due to Biogen Idec International GMBH as a sublicensing fee under our option and license agreement with Biogen dated

March 18, 2009, as amended.

EUSA

In December 2015, we entered into a license agreement with EUSA under which we 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, Australasia and New Zealand for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye. EUSA filed an application with the EMA in February 2016 for approval of marketing authorization for tivozanib in the treatment of RCC.

EUSA is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the licensed territories. With the exception of certain support to be provided by us in connection with the application for marketing approval by the EMA, EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the licensed territories.

Under the license agreement, EUSA made a research and development funding payment to us of $2.5 million in 2015. EUSA is required to make a further research and development funding payment of $4.0 million upon the grant by the European Medicines Agency, or the EMA, of marketing approval for tivozanib for treatment of RCC. We are eligible to receive additional research funding from EUSA, including up to $20.0 million for the Company's phase 3 study in third-line RCC ifEUSA elects to utilize data generated by the study, and up to $2.0 million for a potential phase 1 combination study with a checkpoint inhibitor if EUSA elects to utilize data generated by the study. We will be entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for RCC in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. We are also eligible to receive a payment of $2.0 million in connection with EUSA's filing with the EMA for marketing approval for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as up to $335.0 million upon EUSA's achievement of certain sales thresholds. We are also eligible to receive tiered double digit royalties on net sales, if any, of licensed products in the licensed territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. A percentage of any milestone and royalty payments we receive are due to KHK as a sublicensing fee under the license agreement between us and KHK dated as of December 21, 2006, pursuant to which we acquired exclusive rights to develop and commercialize tivozanib for all human diseases outside of Asia. The research and development funding payments under the EUSA license agreement are not subject to sublicensing payment to KHK.

Novartis

In August 2015, we entered into a license agreement with Novartis, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and our related antibodies that bind to GDF15 worldwide. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide.

Novartis made an upfront payment to us of $15.0 million in September 2015. We are also eligible to receive (a) up to $53 million in potential clinical milestone payments and up to $105 million in potential regulatory milestone payments tied to the commencement of clinical trials and to regulatory approvals of products developed under the license agreement in the United States, the European Union and Japan; and (b) up to $150 million in potential sales based milestone payments based on annual net sales of such products. Upon commercialization, we are eligible to receive tiered royalties on net sales of approved products ranging from the high single digits to the low double digits. Novartis has responsibility under the license agreement for the development, manufacture and commercialization of the licensed antibodies and any resulting approved therapeutic products. In December 2015, Novartis also exercised its right under the license agreement to acquire our inventory of clinical quality drug substance, reimbursing us approximately $3.5 million for such existing inventory.

Pharmstandard Group

In August 2015, we entered into an exclusive license agreement with Pharmstandard, under which we granted Pharmstandard the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States for all conditions excluding non-oncologic ocular conditions.

In June 2016, following unsuccessful efforts to renegotiate certain terms of the Pharmstandard license agreement, Pharmstandard notified us that due to economic and market changes in Russia it was exercising its right to terminate the license agreement effective September 9, 2016. Upon termination of the license agreement, the licenses to tivozanib we granted to Pharmstandard will terminate, all product rights and regulatory documents will be transferred to us, Pharmstandard will no longer be responsible for the development and commercialization of tivozanib, and Pharmstandard will have no further payment obligations under the license agreement except with respect to payments that accrued prior to the effective date of the termination.

Pharmstandard filed an application for marketing authorization in Russia for tivozanib for the treatment of renal cell carcinoma that was accepted by the Ministry of Health of the Russian Federation in February 2016. We expect this application to be withdrawn following Pharmstandard's termination notice. We plan to seek a new partner for the development and commercialization of tivozanib in these territories.

Ophthotech

In November 2014 we entered into a research and exclusive option agreement with Ophthotech.

Pursuant to this agreement, we granted to Ophthotech a license to perform certain research and development activities during the option period. These activities include formulation work for ocular administration, preclinical research and the conduct of a Phase 1/2a, proof of concept clinical trial of a product containing tivozanib in patients with wet age-related macular degeneration.

We also granted Ophthotech an exclusive option to license tivozanib outside of Asia for the diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

Ophthotech paid us $0.5 million in consideration for the grant of the option. Such amount is non-refundable and not creditable against any other amounts due under the agreement. We are obligated to make available to Ophthotech, at no cost, certain quantities of tivozanib hydrochloride solely for research purposes, including manufacturing additional quantities of tivozanib in the event stability data indicates that the current supply will expire prior to the end of February 2017. A percentage of all payments we receive from Ophthotech are due to KHK as a sublicensing fee under the KHK agreement.

Biodesix

In April 2014, we entered into a worldwide agreement with Biodesix to develop and commercialize ficlatuzumab, our HGF inhibitory antibody, with BDX004, a proprietary companion diagnostic test developed by Biodesix and based upon an exploratory analyses with VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced NSCLC.

Pursuant to a joint development plan, we retain primary responsibility for clinical development of ficlatuzumab in a proof of concept clinical study of ficlatuzumab for NSCLC in which VeriStrat will be used to select clinical trial subjects. The trial is fully funded by Biodesix up to a cap of $15.0 million, other than manufacturing costs for the trial, which are shared equally. Under the agreement, after the cap is reached we and Biodesix share equally in any additional costs of the NSCLC trial. We would each be responsible for 50% of development and regulatory costs associated with any future clinical trials we and Biodesix decide to undertake, including all milestone payments and royalties payable to third parties, if any. Biodesix is responsible for all of the costs associated with development and registration of BDX004. Under the Biodesix agreement, subject to regulatory approval, we would lead worldwide commercialization of ficlatuzumab.

St. Vincent’s Hospital

In July 2012, we entered into a license agreement with St. Vincent’s Hospital Sydney Limited, which we refer to as St. Vincent’s, under which we obtained an exclusive, worldwide license to research, develop, manufacture and commercialize products for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which is also known as GDF15. We believe GDF15 is a novel target for cachexia and we are exploiting this license in our AV-380 program for cachexia. Under the agreement, we have the right to grant sublicenses subject to certain restrictions. We have a right of first negotiation to obtain an exclusive license to certain improvements that St. Vincent’s or third parties may make to licensed therapeutic products. Under the license agreement, St. Vincent’s also granted us non-exclusive rights for certain related diagnostic products and research tools.

In August 2015, in connection with the execution of our license agreement with Novartis, we entered into an amended and restated agreement with St. Vincent’s, pursuant to which we made an upfront payment to St. Vincent’s of $1.5 million. St. Vincent’s is also eligible to receive up to approximately $18.9 million in connection with development and regulatory milestones. We made a $0.4 million milestone payment to St. Vincent’s during the six months ended June 30, 2016 related to the selection of a development candidate. Royalties for approved products resulting from the license agreement will also be payable to St. Vincent’s, and we and Novartis will share that obligation equally.

Astellas Pharma

In February 2011, we entered into a collaboration and license agreement with Astellas Pharma Inc., or Astellas, to develop and commercialize tivozanib for the treatment of a broad range of cancers. On February 12, 2014, Astellas exercised its right to terminate the agreement. The termination of the agreement became effective August 11, 2014, at which time tivozanib rights returned to us. In accordance with the collaboration and license agreement, we and

Astellas agreed to equally share committed development costs, including the costs of completing certain tivozanib clinical development activities that had been initiated as part of our partnership with Astellas.

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, or Biogen Idec, regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases in humans outside of North America. Under the agreement, we were responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, will generate data sufficient to support advancement to a phase 3 clinical trial. In March 2014, we amended our agreement with Biogen Idec, whereby Biogen Idec agreed to the termination of its rights and obligations under the agreement, including Biogen Idec’s option

to (i) obtain a co-exclusive (with us) 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, we retain worldwide rights to AV-203, a clinical stage ErbB3-targeted antibody. Pursuant to the amendment, we were obligated to in good faith use reasonable efforts to seek a collaboration partner to fund further development and commercialization of ErbB3-targeted antibodies. We satisfied this obligation in March 2016 upon entering into our license agreement with CANbridge. We are obligated to pay Biogen Idec a percentage of milestone payments we receive under the CANbridge agreement and single digit royalty payments on net sales related to the sale of AV-203, up to cumulative maximum amount of $50.0 million.

Kyowa Hakko Kirin

In December 2006, we entered into a license agreement with KHK under which we obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world except for Asia, where KHK has retained rights to tivozanib. Under the license agreement, we obtained exclusive rights in our territory under certain KHK patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. We and KHK 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 license agreement.

Under the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize tivozanib in our territory, including meeting certain specified diligence goals. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in our territory, neither we nor any of our subsidiaries has the right to conduct certain clinical trials of, seek marketing approval for or commercialize any other cancer product that also works by inhibiting the activity of the VEGF receptor.

Upon entering into the license agreement with KHK, we made a one-time cash payment in the amount of $5.0 million. In March 2010, we made a $10.0 million milestone payment to KHK in connection with the dosing of the first patient in our phase 3 clinical trial of tivozanib. We made a $22.5 million payment to KHK during the year ended December 31, 2011 related to the up-front license payment received under Astellas agreement In December 2012, we made a $12.0 million milestone payment to KHK in connection with the acceptance by the FDA of our NDA filing for tivozanib. The total remaining payments for clinical and regulatory milestones under our license agreement with KHK are $38.0 million, in the aggregate, provided that the associated clinical and regulatory milestones specific to licensed territories will be replaced by a specified percentage of any non-research and development amounts we receive from any third party in the event we sublicense our rights under the agreement.

We are required to pay to KHK 30% of certain amounts we receive from sublicensees, including up-front license fees, milestone payments and royalties, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

Financial Overview

We have devoted substantially all of our resources to our drug development efforts, including research and development, conducting clinical trials for our product candidates, manufacturing, protecting our intellectual property and the general and administrative functions relating to these operations. We have generated no revenue from product sales through June 30, 2016, and through such date have principally funded our operations through the proceeds from

our strategic partnerships, sales of stock to investors and loan agreements with Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.) and certain of its affiliates, which we sometimes refer to collectively as Hercules.

We do not have a history of being profitable and, as of June 30, 2016, we had an accumulated deficit of $511.3 million. We anticipate that we will continue to incur significant operating costs over the next several years as we continue our planned development activities for our preclinical and clinical products. We will need additional funding to support our operating activities, and the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

Revenue

To date, we have not generated any revenue from product sales. All of our revenue to date has been derived from license fees, milestone payments, premium over the fair value of convertible preferred shares sold to our strategic partners, and research and development payments received from our strategic partners.

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development reimbursements, milestone and other payments received under our strategic partnerships, and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. We do not expect to generate revenue from product sales in the near term. If we or our strategic partners fail to complete the development of our drug candidates in a timely manner or obtain 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. These expenses consist primarily of:

- employee-related expenses, which include salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials and a substantial portion of our preclinical studies;
- the cost of acquiring and manufacturing drug development related materials;
- the cost of completing certain tivozanib clinical development activities that were initiated as part of our prior partnership with Astellas;
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and depreciation of fixed assets;
    - license fees for, and milestone payments related to, in-licensed products and technology; and
- costs associated with outsourced development activities, regulatory approvals and medical affairs.

We expense research and development costs as incurred. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

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

We anticipate that research and development expenses will increase in 2016 as compared to 2015 due to the commencement of enrollment in May 2016 in the TIVO-3 trial and the potential commencement of a phase 1/2 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC.

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and laboratory supplies, to each program based on the personnel resources allocated to such program. Facilities, depreciation, stock-based compensation, research and development management and research and development support services are not allocated among programs and are considered overhead. Below is a summary of our research and development expenses for the three months and six months ended June 30, 2016 and 2015:

	Three Months Ended	Six Months Ended
	June 31,	June 30,

	2016	2015	2016	2015
	(in thousands)		(in thousands)	
Tivozanib	$5,273	$993	$10,257	$2,438
AV-380 Program in Cachexia	38	282	464	757
Ficlatuzumab	104	—	353	—
AV-203	9	79	79	366
Other pipeline programs	—	—	—	11
Other research and development	—	—	—	10
Overhead	180	487	423	954
Total research and development expenses	$5,604	$1,841	$11,576	$4,536

Tivozanib

We have pursued partnering options to fund further tivozanib development in appropriate clinical settings outside of our strategic focus. In February 2016, our strategic partner EUSA submitted an application for marketing authorization for tivozanib for the treatment of RCC to the European Medicines Agency. EUSA is responsible for all activities and costs associated with the further development and commercialization of tivozanib within the licensed territories. We continue to share the costs of development activities to which we and Astellas were committed at the time the Astellas partnership was terminated.

In May 2016, we initiated TIVO-3, an additional phase 3 trial of tivozanib vs. sorafenib. TIVO-3, which is expected to enroll approximately 322 patients in the refractory RCC setting, will use PFS as the primary endpoint and OS as a secondary endpoint, and is designed to address the OS concerns presented in the June 2013 complete response letter from the FDA and to support a request for approval of tivozanib as a third-line treatment and as a first-line treatment. We expect the total estimated costs of this trial to be approximately $28.0 - $30.0 million through completion. We are also planning to conduct a phase 1/2 trial of tivozanib in combination with a PD-1 inhibitor for the treatment of RCC, for which costs could be in the range of $2.0 - $2.5 million.

AV-380 Program in Cachexia

In August 2015, we entered into a license agreement with Novartis, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and related AVEO antibodies that bind to Growth Differentiation Factor 15 worldwide. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide. We do not expect to incur any significant costs related to AV-380 in future periods beyond any milestone fees and royalties payable to St. Vincent's pursuant to our in-licensing agreement, which comprises substantially all of the costs incurred during the six months ended June 30, 2016.

AV-203

In March 2014, we regained our worldwide rights from Biogen Idec to develop, manufacture and commercialize AV-203. In March 2016, we entered into a collaboration and license agreement with CANbridge, under which we granted CANbridge the exclusive right to develop and commercialize AV-203 in all countries other than the United States, Canada and Mexico. CANbridge is responsible for all costs of developing and commercializing AV-203 within the licensed territory. For a period of time following the completion of certain proof-of-concept clinical studies by CANbridge involving the use of AV-203 for the treatment of squamous cell esophagus cancer, we agreed to negotiate exclusively with CANbridge for (a) the right to co-develop ErbB3 inhibitory antibody products for the treatment of squamous cell esophagus cancer or (b) the right to include the United States, Canada and Mexico as part of the licensed territories. We do not expect to incur any significant costs related to AV-203 prior to CANbridge's completion of a proof-of-concept clinical study.

Ficlatuzumab

In April 2014, we entered into a worldwide agreement with Biodesix to develop and commercialize ficlatuzumab, our potent HGF inhibitory antibody, with BDX004, a proprietary companion diagnostic test, developed by Biodesix and based upon an exploratory analyses with VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced NSCLC. Pursuant to the agreement, Biodesix will provide up to $15.0 million for a phase 2 trial of ficlatuzumab in combination with erlotinib in first-line advanced NSCLC patients selected using BDX004 and fund the further development and registration of BDX004 as a companion diagnostic. Any manufacturing costs incurred are shared equally. After the completion of the phase 2 trial, any additional development, regulatory or commercial expenses for ficlatuzumab will be equally shared. Due to the unpredictable nature of clinical development, we are unable to estimate with any certainty the costs we will incur in

the future development of ficlatuzumab.

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 quality of the product candidate's early clinical data, 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; and
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims.

As a result of the uncertainties associated with developing drugs, including those discussed above, we are unable to determine the 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. 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.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, corporate development, information technology, legal and human resource functions. Other general and administrative expenses include facility costs not otherwise included in research and development expenses, patent filing, prosecution and defense costs and professional fees for legal, consulting, pre-commercialization activities, auditing and tax services.

We anticipate that our general and administrative expenses will decrease in 2016 as compared to 2015 due to our relocation to a smaller facility during the second quarter of 2015 and decreased legal costs associated with ongoing shareholder litigation and our recently-settled U.S. Securities and Exchange Commission, or SEC, investigation described in this report under the heading "Legal Proceedings" below in Part II—Item 1.

Warrants Issued in Connection with Private Placement

We account for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. These warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a non-cash component of other expense, until the earlier of their exercise or expiration or upon the completion of a liquidation event.

Interest Expense, Net

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

Income Taxes

We calculate our provision for income taxes on ordinary income based on our projected annual tax rate for the year. As of June 30, 2016, we are forecasting a net loss for the year ended December 31, 2016, and since we maintain a full valuation allowance on all of our deferred tax assets, we have recorded no income tax benefit in the current quarter. For the six months ended June 30, 2016, we recorded a $0.1 million provision for income taxes related to withholding taxes incurred in a foreign jurisdiction.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued clinical expenses, and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we and our management believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in the notes to our condensed consolidated financial statements appearing elsewhere in this report. There have been no material changes to our critical accounting policies during the six-month period ended June 30, 2016. Please refer to Part II, Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations”, of our annual report on Form 10-K for the fiscal year ended December 31, 2015 for further discussion of our critical accounting policies and significant judgments and estimates.

Results of Operations

Comparison of Three Months Ended June 30, 2016 and 2015

The following table summarizes the results of our operations for each of the three months ended June 30, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

	Three Months Ended			
	June 30, 2016	2015	Increase/ (decrease)	%
	(in thousands)			
Revenue	$193	$134	$ 59	44 %
Operating expenses:				
Research and development	5,604	1,841	3,763	204 %
General and administrative	1,731	2,889	(1,158)	(40)%
Restructuring and lease exit	—	25	(25)	(100)%
Total operating expenses	7,335	4,755	2,580	54 %
Loss from operations	(7,142)	(4,621)	(2,521)	55 %
Interest expense, net	(468)	(626)	158	(25)%
Change in fair value of warrant liability	(996)	—	(996)	— %
Other expense	—	(209)	209	(100)%
Loss before income taxes	(8,606)	(5,456)	(3,150)	58 %
Income tax provision	—	—	—	— %
Net loss	$(8,606)	$(5,456)	$ (3,150)	58 %

The following table sets forth revenue for the three months ended June 30, 2016 and 2015:

Revenue	Three Months Ended June 30, 2016	2015	Increase/ (decrease)	%
	(in thousands)			
Strategic Partner:				
CANbridge	$28	$—	$ 28	100
EUSA	99	—	0	100 %
Biogen Idec	—	76	(76)	(100)%
Pharmstandard	37	—	37	100 %
Ophthotech	29	58	(29)	(50)%
	$193	$134	$ (40)	(30)%

Revenue. Revenue for the three months ended June 30 2016 was $0.2 million compared to $0.1 million for the three months ended June 30, 2015, an increase of approximately $0.1 million. The increase was primarily due to $0.1 million in revenue recognized in the second quarter of 2016 in connection with our out-licensing agreement with EUSA, which was executed in December 2015.

Research and development. Research and development, or R&D, expenses for the three months ended June 30, 2016 were $5.6 million compared to $1.8 million for the three months ended June 30, 2015, an increase of $3.8 million or 204%. The increase was primarily attributable to an increase in tivozanib clinical trial costs in connection with our TIVO-3 phase 3 trial in renal cell carcinoma that commenced enrollment and patient treatment in May 2016. For the remainder of 2016, we anticipate that research and development expenses will continue to increase as we advance enrollment in the TIVO-3 trial and potentially commence a phase 1/2 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC.

General and administrative. General and administrative expenses for the three months ended June 30, 2016 were $1.7 million compared to $2.9 million for the three months ended June 30, 2015, a decrease of $1.2 million or 40%. The decrease was primarily the result of a $0.4 million decrease in external legal costs associated with various ongoing legal matters, a $0.6 million decrease in employee compensation, consulting, facilities and IT costs following our decreased headcount and the reduction of our utilized facility space following our 2015 restructuring. For the remainder of 2016, we anticipate that general and administrative expenses will remain at current levels.

Change in fair value of warrant liability. The loss from the change in the fair value of our warrant liability from the time of inception for the three months ended June 30, 2016 was $1.0 million. In May 2016, we issued warrants in connection with a private placement financing and recorded the warrants as a liability. The changes in the fair value at the end of each reporting date are recorded as a non-cash gain or loss in the Statements of Operations and Comprehensive Income (Loss).

Interest expense, net. Interest expense, net for the three months ended June 30, 2016 was $0.4 million compared to $0.6 million for the three months ended June 30, 2015. The decrease was primarily attributable to the decrease in the outstanding balance on our loan with Hercules. For the remainder of 2016, we anticipate that interest expense will increase in connection with the additional loan proceeds received from Hercules under the May 2016 amended Loan Agreement and corresponding issuance of warrants.

Comparison of Six Months Ended June 30, 2016 and 2015

The following table summarizes the results of our operations for each of the six months ended June 30, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

	Six Months Ended			
	June 30, 2016	2015	Increase/ (decrease)	%
	(in thousands)			
Revenue	$1,396	$268	$ 1,128	421 %
Operating expenses:				
Research and development	11,576	4,536	7,040	155 %
General and administrative	4,203	6,144	(1,941)	(32)%
Restructuring and lease exit	—	4,358	(4,358)	(100)%
Total operating expenses	15,779	15,038	741	5 %
Loss from operations	(14,383)	(14,770)	387	(3)%
Interest expense, net	(837)	(1,337)	500	(37)%
Change in fair value of warrant liability	(996)	—	(996)	— %
Other expense	—	(223)	223	(100)%
Loss before income taxes	(16,216)	(16,330)	114	(1)%
Income tax provision	(100)	—	(100)	100 %

Net loss	$(16,316)	$(16,330)	$ 14	(0)%

The following table sets forth revenue for the six months ended June 30, 2016 and 2015:

Revenue	Six Months Ended June 30, 2016	2015	Increase/ (decrease)	%
	(in thousands)			
Strategic Partner:				
CANbridge	$1,028	$—	$ 1,028	100
EUSA	197	—	0	100%
Biogen Idec	38	152	(114)	(75)%
Pharmstandard	75	—	75	100%
Ophthotech	58	116	(58)	(50)%
	$1,396	$268	$ 931	347%

Revenue. Revenue for the six months ended June 30 2016 was $1.4 million compared to $0.3 million for the six months ended June 30, 2015, an increase of approximately $1.1 million. The increase was primarily due to the $1.0 million upfront payment received in connection with a collaboration and license agreement with CANbridge entered into in March 2016.

Research and development. Research and development, or R&D, expenses for the six months ended June 30, 2016 were $11.6 million compared to $4.5 million for the six months ended June 30, 2015, an increase of $7.0 million or 155%. The increase was primarily attributable to an increase in tivozanib clinical trial costs and drug product manufacturing in connection with our TIVO-3 phase 3 trial in renal cell carcinoma that commenced enrollment and patient treatment in May 2016. For the remainder of 2016, we anticipate that research and development expenses will continue to increase as we advance enrollment in the TIVO-3 trial and potentially commence a phase 1/2 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC.

General and administrative. General and administrative expenses for the six months ended June 30, 2016 were $4.2 million compared to $6.1 million for the six months ended June 30, 2015, a decrease of $1.9 million or 32%. The decrease was primarily the result of a $0.7 million decrease in external legal costs associated with various ongoing legal matters, a $1.1 million decrease in employee compensation, consulting, facilities and IT costs following our decreased headcount and the reduction of our utilized facility space following our 2015 restructuring. For the remainder of 2016, we anticipate that general and administrative expenses will remain at current levels.

Restructuring and lease exit. Restructuring and lease exit expenses for the six months ended June 30, 2016 and 2015 were $0 and $4.4 million, respectively. The expenses incurred during the six months ended June 30, 2015 related to the January 2015 restructuring, which was substantially completed in March 2015. As part of this restructuring, we eliminated our internal research function, reducing our headcount by approximately 40 positions.

Change in fair value of warrant liability. The loss from the change in the fair value of our warrant liability from the time of inception for the six months ended June 30, 2016 was $1.0 million. In May 2016, we issued warrants in connection with a private placement financing and recorded the warrants as a liability. The changes in the fair value at the end of each reporting date are recorded as a non-cash gain or loss in the Statements of Operations and Comprehensive Income (Loss).

Interest expense. Interest expense for the six months ended June 30, 2016 was $0.8 million compared to $1.3 million for the six months ended June 30, 2015. The decrease was primarily attributable to the decrease in the outstanding balance on our loan with Hercules. For the remainder of 2016, we anticipate that interest expense will increase in connection with the additional loan proceeds received from Hercules under the May 2016 amended Loan Agreement and corresponding issuance of warrants.

Income Tax Provision. Income tax provision for the six months ended June 30, 2016 was $0.1 million compared to $0 for the six months ended June 30, 2015. The increase in the income tax provision relates to withholding taxes incurred in a foreign jurisdiction related income earned from our licensing agreement with CANbridge.

Liquidity and Capital Resources

We have funded our operations principally through the sale of equity securities sold in private placements and underwritten public offerings, revenue and expense reimbursements from strategic partnerships, debt financing and interest income. In May 2016, we raised approximately $20.3 million in net cash proceeds, including $15.4 million in net proceeds from a private placement of 17,642,842 units, each including one share of our common stock and a warrant to purchase one share of our common stock, and $4.9

million in net proceeds from additional borrowings under our Hercules loan agreement. As of June 30, 2016, we had cash, cash equivalents and marketable securities of approximately $39.5 million. Currently, our funds are invested in money market funds, U.S. government agency securities, and corporate debt securities, including commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Six Months Ended June 30,	
	2016	2015
	(in thousands)	
Net cash (used in) operating activities	$(14,909)	$(27,250)
Net cash provided by (used in) investing activities	(6,699)	1,188
Net cash provided by (used in) financing activities	20,305	522
Net decrease in cash and cash equivalents	$(1,303)	$(25,540)

Our operating activities used cash of $14.9 million and $27.3 million in the six months ended June 30, 2016 and 2015, respectively. Cash used by operations was due primarily to our net loss adjusted for non-cash items and changes in working capital.

Our investing activities used cash of $6.7 million and provided cash of $1.2 million in the six months ended June 30, 2016 and 2015, respectively. Cash used by investing activities for the six months ended June 30, 2016 was primarily the net result of the purchase of marketable securities, partially offset by the maturities of marketable securities. Cash provided by investing activities for the six months ended June 30, 2015 was primarily the result of the proceeds of maturities of marketable securities and the sale of equipment.

Our financing activities provided cash of $20.3 million and $0.5 million in the six months ended June 30, 2016 and 2015, respectively. In May 2016, we raised approximately $20.3 million in net cash proceeds, including $15.4 million in net proceeds from a private placement of 17,642,842 units, each including one share of our common stock and a warrant to purchase one share of our common stock, and $4.9 million in net proceeds from additional borrowings under our Hercules loan agreement. In the six months ended June 30, 2015, we raised approximately $6.1 million in net proceeds from the sale of our common stock, including $5.8 million under our ATM facility with FBR and $0.3 million from the exercise of common stock options, offset by $5.6 million in principal payments under our Hercules loan agreement.

Private Placement / PIPE Warrants

In May 2016, we entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which we sold 17,642,482 units, at a price of $0.965 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of our common stock and a warrant to purchase one share of our common stock (the “PIPE Warrants”). The PIPE Warrants have an exercise price of $1.00 per share and are exercisable in any manner at any time for a period of five years from the date of issuance. Certain of our directors and executive officers purchased an aggregate of 544,039 units in this offering at the same price as the other investors. The net offering proceeds to us were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by us.

The PIPE Warrants contain a provision giving the warrant holder the option to receive cash, equal to the fair value of the remaining unexercised portion of the warrant, as cash settlement in the event that there is a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, Distinguishing Liabilities from Equity requires that these warrants be classified as a liability and not as equity. Accordingly, we recorded a warrant liability in the amount of approximately $9.3 million. The fair value of these warrants has been determined using the Black Scholes valuation model, and the changes in the fair value at the time of each reporting date are recorded in the Statements of Operations and Comprehensive Income (Loss). During the three months ended June 30, 2016, as a result of the fair value adjustment of the warrant liability, we recorded a non-cash loss on the increase in the fair value of approximately $1.0 million in the Statements of Operations and Comprehensive Income (Loss). As of June 30, 2016, none of the PIPE Warrants have been exercised.

At-The-Market Issuance Sales Agreement with FBR

In February 2015, we entered into an at-the-market issuance sales agreement, which we refer to as the Sales Agreement, with FBR & Co., or FBR, (formerly MLV & Co. LLC), pursuant to which we could issue and sell shares of our common stock from time to time up to an aggregate amount of $17.9 million, at our option, through FBR as our sales agent. Sales of common stock through FBR may be 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, including by means of ordinary brokers’ transactions at market prices, in block transactions or as otherwise

agreed by the Company and FBR. Subject to the terms and conditions of the Sales Agreement, FBR will use commercially reasonable efforts to sell our common stock based upon our instructions (including any price, time or size limits or other customary parameters or conditions we may impose). We are not obligated to make any sales of common stock under the Sales Agreement. Any shares sold will be sold pursuant to an effective shelf registration statement on Form S-3. We are required to pay FBR a commission of up to 3% of the gross proceeds. The Sales Agreement may be terminated by us at any time.

On May 7, 2015, we filed a shelf registration statement on Form S-3 with the SEC, which we refer to as the 2015 Shelf. The 2015 Shelf covers the offering, issuance and sale of up to $100 million of our common stock, preferred stock, debt securities, warrants and/or units. The 2015 Shelf was filed to replace our existing $250 million shelf registration statement, which expired at the end of May 2015, and which we refer to as the 2012 Shelf. On May 7, 2015, we also amended the Sales Agreement to provide for the offering, issuance and sale of up to $15 million of our common stock under the 2015 Shelf. The prior at-the-market offering initiated under the original Sales Agreement expired along with the 2012 Shelf. As of June 30, 2016, we have sold approximately 5.9 million shares pursuant to the Sales Agreement, as amended, resulting in proceeds of approximately $10.2 million, net of commissions and issuance costs. No shares have been sold during the three and six months ended June 30, 2016.

Approximately $9.1 million remains available for sale under the Sales Agreement.

Credit Facilities.

On May 28, 2010, we entered into a loan and security agreement (the “Loan Agreement”) with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth (collectively, “Hercules”). The Loan Agreement was subsequently amended in March 2012, September 2014 (the “2014 Amendment”) and May 2016 (the “2016 Amendment”). Amounts borrowed under the March 2012 Amendment were repaid in full in 2015.

Pursuant to the 2014 Amendment, we received additional loan proceeds from Hercules in the amount of $10.0 million and were not required to commence principal payments until May 1, 2016. An end-of-term payment of approximately $0.5 million continues to be due on January 1, 2018 or on such earlier date if the loan is prepaid.

Pursuant to the 2016 Amendment, we received additional loan proceeds from Hercules in the amount of $5.0 million, which increased the aggregate outstanding principal balance under the Loan Agreement to $15.0 million. We are not required to commence principal payments on the $15 million loan until July 1, 2017, at which time we will be required to make 30 equal monthly payments of principal and interest through December 2019. An end-of-term payment of approximately $0.2 million is due on December 1, 2019. The 2016 Amendment includes a financial covenant that requires us to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of our Phase 3 TIVO-3 trial.

Under the 2016 Amendment, we may, at our request during any time from March 1, 2017 through June 30, 2017, draw down an additional $5.0 million in funding. This funding is contingent upon us: (i) achieving satisfactory developmental progression on a minimum of two (2) clinical programs (other than the Phase 3 TIVO-3 trial) that are either managed directly by us or funded, in whole or in part, by us and (ii) having an unrestricted cash position greater than or equal to $25.0 million on the date of the draw down request. If we draw down the additional $5.0 million in funding, the commencement of principal payments on the aggregate $20.0 million loan balance will be deferred by six months from July 1, 2017 until January 1, 2018.

We must make interest payments on the principal balance of the loan each month it remains outstanding. Per annum interest is payable on the loan balance at the greater of 11.9% and an amount equal to 11.9% plus the prime rate minus 4.75%, as determined daily, provided however, that the per annum interest rate shall not exceed 15.0%. Our annual interest rate as of June 30, 2016 was 11.9%.

We have determined that the risk of subjective acceleration under the material adverse events clause included in this loan and security agreement is remote and, therefore, have classified the outstanding principal amount in current and long-term liabilities based on the timing of scheduled principal payments. As of June 30, 2016, we are in compliance with all of the financial covenants and through the date of this filing, the lenders have not asserted any events of default under the loan. We do not believe that there has been a material adverse change as defined in the loan agreement.

The loans are secured by a lien on all of our personal property (other than intellectual property), whether owned as of, or acquired after, the date of the Loan Agreement.

Operating Capital Requirements.

We anticipate that we will continue to incur significant operating losses for the next several years as we incur expenses to continue to execute on our clinical development strategy to advance our clinical stage assets. We will require substantial funds to continue our development programs and to fulfill our planned operating goals. In particular, our currently planned operating and capital requirements include the need for substantial working capital to support our development activities for tivozanib. For example, we estimate that the remaining costs for the TIVO-3 trial for RCC could be in the range of $28-30 million in the aggregate through 2018. We are also designing a phase 1/2 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC for which costs could be in the range of $2.0-$2.5 million. Moreover, we have future payment obligations and cost-sharing arrangements under certain of our collaboration and license agreements. For example, under our agreements with KHK and St. Vincent's, we are required to make certain clinical and regulatory milestone payments, have royalty obligations with respect to product sales and are required to pay a specified percentage of sublicense revenue in certain instances. Moreover, under our agreement with Biodesix, we are obligated to share any costs for the phase 2 FOCAL study that exceed $15 million, and to share any manufacturing and future development costs. Accordingly, we will need substantial additional funding in connection with our planned operations. If we are unable to raise capital when needed or on attractive terms, or if we are unable to procure partnership arrangements to advance our programs, we would be forced to delay, reduce or eliminate our research and development programs and any future commercialization efforts.

We believe that our approximate $39.5 million in cash, cash equivalents and marketable securities at June 30, 2016 could allow us to fund our planned operations into the fourth quarter of 2017. This estimate assumes no receipt of milestone payments from our partners or related payment of potential licensing milestones to third parties, no additional funding from new partnership agreements, no equity financings, no debt financings, no accelerated repayment of our term loan and no further sales of equity under our Sales Agreement with FBR.

In addition to our approximate $39.5 million in existing cash resources at June 30, 2016, we have significant potential milestone payments that could be received from four of our business partnerships through 2017, an option to receive an additional $5 million in loan proceeds under our Loan Agreement with Hercules and a corresponding six-month deferral of principal payments, subject to the terms of the Loan Agreement, and access to up to $9.1 million in gross proceeds from potential sales of our common stock under our Sales Agreement with FBR. If we are unable to obtain sufficient cash resources from one or more of these or other sources, we may not be able to maintain compliance with the financial covenant under our Loan Agreement with Hercules (refer to Note 6 in the condensed consolidated financial statements). Moreover, there can be no assurance that we will receive cash proceeds from any of these potential resources.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements and the period in which we will have working capital to fund our operations. Accordingly, the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

Our future funding requirements will depend on many factors, including, but not limited to:

- 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 conducting preclinical and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our loan agreement with Hercules or under any other agreements with third parties;
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the outcome of legal actions against us, including the current lawsuits described under “Part II, Item 1—Legal Proceedings”;

- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

If our available cash and cash equivalents are insufficient to satisfy our liquidity requirements, or if we identify additional opportunities to do so, 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. We will require additional capital beyond our currently forecasted amounts. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to:

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

Contractual Obligations and Commitments

In May 2016, we amended our Loan Agreement with Hercules and received $5.0 million in additional loan proceeds, which increased the aggregate outstanding principal balance under the Loan Agreement to $15.0 million (refer to Note 6 in the condensed consolidated financial statements).

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, 2015 filed with the SEC on March 15, 2016.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of June 30, 2016, we had cash, cash equivalents and marketable securities of $39.5 million, consisting of cash on deposit with banks, money market funds, U.S. government agency securities, and corporate debt, including commercial paper. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term cash equivalents. Our cash equivalents are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We have the ability to hold our cash equivalents until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments. We do not currently have any auction rate securities.

We are also exposed to market risk related to change in foreign currency exchange rates. We contract with contract research organizations and investigational sites that are located around the world. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk.

Item 4. Controls and Procedures.

Our management, with the participation of our President and Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2016. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our President and Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer) concluded that as of June 30, 2016, 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 we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended June 30, 2016 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

Two class action lawsuits have been filed against us and certain of our former officers and members of our board of directors, (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer and Ronald DePinho), in the United States District Court for the District of Massachusetts, one captioned Paul Sanders v. Aveo Pharmaceuticals, Inc., et al., No. 1:13-cv-11157-JLT, filed on May 9, 2013, and the other captioned Christine Krause v. AVEO Pharmaceuticals, Inc., et al., No. 1:13-cv-11320-JLT, filed on May 31, 2013. On December 4, 2013, the District Court consolidated the complaints as In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC, and an amended complaint was filed on February 3, 2014. The amended complaint purported to be brought on behalf of shareholders who purchased our common stock between January 3, 2012 and May 1, 2013. The amended complaint generally alleged that we and certain of our present and former officers and directors violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the phase 3 trial design and results for our TIVO-1 study in an effort to lead investors to believe that the drug would receive approval from the FDA. The lawsuit seeks unspecified damages, interest, attorneys' fees, and other costs. The consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations. We moved to dismiss again, and after a second round of briefing and oral argument, the court ruled in our favor and dismissed the second amended complaint with prejudice on November 18, 2015. The lead plaintiffs have appealed the court's decision to the United States Court of Appeals for the First Circuit. They have also filed a motion to vacate and reconsider the district court's judgment, which we have opposed. We deny any allegations of wrongdoing and intend to continue to vigorously defend against this lawsuit. However, there is no assurance that we will be successful in our defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of the action. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible loss at this time.

On April 4, 2014, Karen J. van Ingen, a purported purchaser of AVEO stock, filed a derivative complaint allegedly on behalf of AVEO in the United States District Court for the District of Massachusetts, Civil Action No. 1:14-cv-11672-DJC, naming AVEO, as a nominal defendant and also naming as defendants present and former members of our board of directors, including Tuan Ha-Ngoc, Henri A. Termeer, Kenneth M. Bate, Anthony B. Evnin, Robert Epstein, Raju Kucherlapati, Robert C. Young, and Kenneth E. Weg. The complaint alleged breach of fiduciary duty and abuse of control between January 2012 and May 2013 with respect to allegedly misleading statements and omissions regarding tivozanib. The lawsuit seeks, among other relief, unspecified damages, costs and expenses, including attorneys' fees, an order requiring us to implement certain corporate governance reforms, restitution from the defendants and such other relief as the court might find just and proper. We filed a motion to dismiss the derivative complaint, and after briefing and oral argument, on March 18, 2015 the Court ruled in our favor and dismissed the case with prejudice. The plaintiff then filed a motion seeking to vacate the Court's order of dismissal and permit filing of an amended complaint, which we opposed, and which the Court denied on June 30, 2015. The plaintiff has appealed the Court's decision to the United States Court of Appeals for the First Circuit. The parties have reached an agreement in principle to settle this matter. The settlement involves certain corporate governance changes and other non-monetary relief. The plaintiffs will seek an award of attorney's fees, which we expect will be paid by insurance. The settlement is subject to negotiation of final documentation and court approval. There can be no assurance that the settlement will be approved by the court.

On July 3, 2013, the staff, or SEC Staff, of the United States Securities and Exchange Commission, or the Commission, served a subpoena on us for documents and information concerning tivozanib, including related communications with the FDA, investors and others. In September 2015, the SEC Staff invited us to discuss the settlement of potential claims asserting that we violated federal securities laws by omitting to disclose to investors the recommendation by the staff of the FDA on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. We agreed to settle those claims for a total amount of $4.0 million, subject to the approval of the Commission.

On March 29, 2016, the Commission filed a complaint against us and three of our former officers in the U.S. District Court for the District of Massachusetts alleging that we misled investors about our efforts to obtain FDA approval for tivozanib. Without admitting or denying the allegations in the Commission's complaint, we consented to the entry of a final judgment pursuant to which we paid the Commission a $4.0 million civil penalty to settle the Commission's claims against us. On March 31, 2016, the District Court entered a final judgment which (i) approved the settlement; (ii) permanently enjoined us from violating Section 17(a) of the Securities Act of 1933, as amended, Sections 10(b) and 13(a) of the Securities Exchange Act of 1934, as amended, and rules 10b-5, 12b-20, 13a-1, 13a-11 and 13a-13 promulgated thereunder; and (iii) ordered us to pay the agreed-to civil penalty. The Commission's action against our three former officers is still pending. We are not a party to any litigation or discussions between the SEC Staff and the former officers, and we can make no assurance regarding the outcome of that action or the Commission's claims against those individuals.

Refer to Footnote 11 in the Notes to Condensed Consolidated Financial Statements for further discussion.

Item 1A. Risk Factors

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Quarterly Report on Form 10-Q and other filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this Quarterly Report on Form 10-Q and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

Risks Related to Our Financial Position and Need for Additional Capital

We anticipate that we will continue to incur significant operating losses for the foreseeable future. It is uncertain if we will ever attain profitability, which would depress the market price of our common stock.

We have incurred a net loss of $16.3 million for the six months ended June 30, 2016 and, as of June 30, 2016, had an accumulated deficit of $511.3 million. To date, we have not commercialized any products or generated any revenues from the sale of products, and absent the realization of sufficient revenues from product sales, we may never attain profitability. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that we will continue to incur significant operating costs over the next several years as we seek to develop our product candidates.

If we do not successfully develop and obtain regulatory approval for our existing and future pipeline of product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales. Even if we do generate product sales, we may never achieve 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.

Our business is in early stage of development, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

All of our product candidates are in early stages of development. We have not yet demonstrated our ability to obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients. Preclinical studies and clinical trials may involve highly uncertain results and a high risk of failure. Moreover, positive data from preclinical studies and clinical trials of our product candidates may not be predictive of results in ongoing or subsequent preclinical studies and clinical trials. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as an early stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To be profitable, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We will require substantial additional funding, 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 will require substantial funds to continue our development programs and to fulfill our planned operating goals. In particular, our currently planned operating and capital requirements include the need for substantial working capital to support our development activities for tivozanib. For example, we estimate that the remaining costs for the TIVO Phase 3 trial for RCC could be in the range of $28-$30 million. We are also designing a phase 1/2 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC for which costs could be in the range of $2.0-$2.5 million. Moreover, we have future payment obligations and cost-sharing arrangements under certain of our collaboration and license agreements. For example, under our agreements with KHK and St. Vincent's, we are required to make certain clinical and regulatory milestone payments, have royalty obligations with respect to product sales and are required to pay a specified percentage of sublicense revenue in certain instances. Moreover, under our agreement with Biodesix, we are obligated to share any costs for the phase 2 FOCAL study that exceed $15 million. Accordingly, we will need substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on

attractive terms, or if we are unable to procure partnership arrangements to advance our programs, we would be forced to delay, reduce or eliminate our research and development programs and any future commercialization efforts.

We believe that our approximate $39.5 million in cash, cash equivalents and marketable securities at June 30, 2016 could allow us to fund our planned operations into the fourth quarter of 2017. This estimate assumes no receipt of milestone payments from our partners or related payment of potential licensing milestones to third parties, no additional funding from new partnership agreements, no equity financings, no debt financings, no accelerated repayment of our term loan and no further sales of equity under our Sales Agreement with FBR.

Because of the numerous risks and uncertainties associated with the development and commercialization of pharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements and the period in which we will have working capital to fund our operations. Accordingly, the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

Our future capital requirements depend on many factors, including:

- 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 developing our product candidates, and conducting preclinical and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our loan agreement with Hercules or under any other agreements with third parties;
- the outcome of legal actions against us, including the current lawsuits described under “Part I, Item 3—Legal Proceedings”;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.

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. We will require additional capital beyond our currently forecasted amounts. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all.

We also expect to seek additional funds through arrangements with collaborators, licensees or other third parties. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or drug candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all.

We anticipate that we will require additional funding. If we are unable to obtain such additional funding on a timely basis, whether through payments under existing or future collaborations or license agreement or sales of debt or equity, we may be required to delay, limit, reduce or terminate our clinical trials or development activities for one or more of our product candidates.

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We may not be successful in establishing and maintaining strategic partnerships to further the development of each of our therapeutic programs. A failure to obtain such partnerships in the near future will 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 major 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 substantial funding, as well as significant capabilities in research, development, marketing and sales

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 development pipeline may be deemed insufficient, our product candidates and programs 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 and programs as having the requisite potential to demonstrate safety and efficacy.

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 and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our product candidates could have an adverse effect on our business or our operating plan, including delaying the development and commercialization of our product candidates.

Moreover, if we fail to establish and maintain additional strategic partnerships related to our product candidates:

- we will have limited resources with which to continue to operate our business and we may not be able to successfully complete any other strategic transactions;
- the development of certain of our product candidates may be terminated or delayed; and
- our cash expenditures related to development of our product candidates would increase significantly and we do not have the cash resources to develop our product candidates on our own.

Risks Related to our Litigation

We and certain of our former officers and present and former directors have been named as defendants in multiple lawsuits that could result in substantial costs and divert management's attention.

We, and certain of our former officers and directors, were named as defendants in a consolidated class action lawsuit initiated in 2013 that generally alleges that we and those individuals violated federal securities laws by making allegedly false and/or misleading statements concerning the development of our drug tivozanib and its prospects for FDA approval. The lawsuit seeks unspecified damages, interest, attorneys' fees, and other costs. The consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations. This second amended complaint was dismissed with prejudice on November 18, 2015. The lead plaintiffs have appealed the court's decision to the United States Court of Appeals for the First Circuit and have also filed a motion to vacate and reconsider the district court's judgment, which we have opposed. Another plaintiff has also filed a derivative complaint, allegedly on our behalf, naming us as a nominal defendant and also naming as defendants present and former members of our board of directors, alleging breach of fiduciary duty and abuse of control on the part of those directors with respect to the same statements at issue in the securities litigation. The derivative complaint seeks, among other relief, unspecified damages, costs and expenses, including attorneys' fees, an order requiring us to implement certain corporate governance reforms, restitution from the defendants and such other relief as the court might find just and proper. The derivative complaint was dismissed with prejudice on March 18, 2015. The plaintiff has appealed the court's decision to the United States Court of Appeals for the First Circuit. We have reached an agreement in principle to settle this matter. The settlement involves certain corporate governance changes and other non-monetary relief. The plaintiffs will seek an award of attorney's fees,

which we expect will be paid by insurance. The settlement is subject to negotiation of final documentation and court approval. There can be no assurance that the settlement will be approved by the court.

We intend to continue to deny the allegations in the class action case and to engage in a vigorous defense of such lawsuit. We intend to resolve the derivative lawsuit in accordance with the proposed settlement. However, we are unable to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us could have a material adverse effect on our financial condition and business. For example, we could incur substantial costs not covered by our liability insurance, suffer a significant adverse impact on our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. In addition, any of these matters could require payments that are not covered by, or exceed the limits of, our available liability insurance, which could have a material adverse effect on our operating results or financial condition.

We have concluded a settlement with the SEC, but the SEC is still pursuing an action against our former officers.

We paid a $4 million to settle a lawsuit filed by the SEC in federal court alleging that we violated federal securities laws by omitting to disclose the recommendation of the staff of the U.S. Food and Drug Administration, on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. See "Part II, Item 1 – Legal Proceedings" for a further discussion of these claims. The SEC also named three of our former officers as defendants in the same lawsuit, and those claims are still pending. We are not a party to, nor are we involved in any litigation or discussions between the SEC and the former officers. However, those individuals may seek advancement of legal expenses or indemnification for any losses, either of which could be material to the extent not covered by our director and officer liability insurance.

Risks Related to Development and Commercialization of Our Drug Candidates

In the near term, we are dependent on the success of tivozanib. If we are unable to initiate or complete the clinical development of, obtain marketing approval for or successfully commercialize tivozanib, either alone or with our collaborators, or if we experience significant delays in doing so, our business could be substantially harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of tivozanib. Our prospects are substantially dependent on our ability, or that of our collaborators, to develop, obtain marketing approval for and successfully commercialize tivozanib in one or more disease indications.

The success of tivozanib will depend on several factors, including the following:

- our ability to secure the substantial additional working capital required to initiate and conduct our planned clinical trials of tivozanib, including the TIVO-3 trial and the planned phase 1/2 PD-1 combination trial in RCC;
- initiation and successful enrollment and completion of clinical trials;
- a safety, tolerability and efficacy profile that is satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the performance of our collaborators;
    - the extent of any required post marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third party raw materials suppliers and manufacturers including with respect to the supply of active pharmaceutical ingredient for tivozanib;
- establishment of arrangements with third party manufacturers to obtain 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 Kyowa Hakko Kirin Co., Ltd.;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third party payors;
- successful identification of biomarkers for patient selection; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of our collaborators. If we are unable to develop, receive marketing approval for and successfully commercialize tivozanib 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.

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, or any collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We, and any collaborators, 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 any collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

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. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation 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. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we or they contemplate, if we, or they, are unable to successfully complete clinical trials of our product candidates or other testing, or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our product candidates, we, or any collaborators, may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, tivozanib or any future product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, tivozanib or any future 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. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

If we, or any collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our current or any future product candidates that we, or any collaborators, may develop, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We, or any collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our current product candidates or any future product candidates that we, or any collaborators, may develop, including:

- 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;
- 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;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third party contractors or those of any collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any collaborators in a timely manner or at all;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we, or any collaborators, may have to delay, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- regulators or institutional review boards may require that we, or any collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- 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.

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

do and impair our ability, or the ability of any collaborators, 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 we, or any collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our or their receipt of necessary regulatory approvals could be delayed or prevented.

We, or any collaborators, may not be able to initiate or continue clinical trials for our current product candidates or any future product candidates that we, or any collaborators, may develop if we, or they, 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 size and nature of the patient population;
- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

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

Results of early clinical trials may not be predictive of results of future late stage clinical trials.

The outcome of early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future 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. For example, in June 2013, the FDA issued a response letter informing us that it would not approve tivozanib for the treatment of first-line advanced renal cell carcinoma based on the study data from our initial Phase 3 trial, and recommended that we perform an additional study that is adequately sized to assure the FDA that there is no adverse effect on overall survival. The design of a clinical trial can determine whether its results will support approval of a product and 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.

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

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for our current product candidates or any future product candidates that we, or any collaborators, may develop.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that we submit for our product candidates or may conclude after review of

our data that our application is insufficient to obtain marketing approval of our product candidate. If the FDA does not accept or approve NDAs for any of our product candidates, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates or any companion diagnostics, generating revenues and achieving and sustaining profitability. If any of these outcomes occurs, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if any product candidates that we, or any collaborators, may develop receive 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.

Clinical trials of any product candidates that we, or any collaborators, may develop will be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any collaborator, 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. If, following approval of a product candidate, we, or others, discover that the 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 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 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 collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

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

Even if our current product candidates, or any future product candidates that we, or any collaborators, may develop receives marketing approval, it 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, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but 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 our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies;

- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first , second or third line therapy;
- our ability, or the ability of any collaborators, to offer the product for sale at competitive prices;
- the product's 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 distribution or use restrictions, contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third party payors.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates if approved.

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to build focused capabilities to commercialize development programs for certain indications where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to effectively promote the product with a targeted sales team. The development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

In certain indications, we seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

If we are unable to successfully develop companion diagnostics for certain of our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of these therapeutics.

A component of our business strategy may be to develop, in collaboration with a third party, companion diagnostics for some of our therapeutic product candidates. There has been limited success to date industry-wide in developing companion diagnostics. To be successful, our collaborator will need to address a number of scientific, technical, regulatory and logistical challenges. We have limited experience in the development of diagnostics and may not be successful in developing appropriate diagnostics to pair with any

of our therapeutic product candidates. The FDA and similar regulatory authorities outside the United States are generally expected to regulate companion diagnostics as medical devices. In each case, companion diagnostics require separate regulatory approval prior to commercialization. For example, BDX004, our companion diagnostic test for ficlatuzumab in our FOCAL study, requires separate approval by the FDA, for which we must rely on Biodesix to obtain. In addition, we require a commercializable companion diagnostic assay to identify patients with low NRP-1 in order to proceed with the development of tivozanib in CRC. We expect to rely in part on third parties for the design, development and manufacture of any companion diagnostic. If we, or any third parties that we engage to

assist us, are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so, the development of our therapeutic product candidates may be adversely affected, our therapeutic product candidates may not receive marketing approval and we may not realize the full commercial potential of any therapeutics that receive marketing approval. As a result, our business would be harmed, possibly materially.

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. 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 objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. We expect any product candidate that we commercialize with our strategic partners will compete with existing, market-leading products.

There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to our products. A number of multinational pharmaceutical companies, as well as large biotechnology companies, including, but not limited to, Roche Laboratories, Inc., Pfizer Inc., Bayer HealthCare AG, Amgen, Inc., Eli Lilly and Company, GlaxoSmithKline plc, GTx, Inc., Helsinn and XBiotech, Novartis, Bristol-Myers Squibb, Merck, Merrimack Pharmaceuticals, Inc., Arqule, Inc., Exelixis, Inc., Easai Co., Ltd., AstraZeneca, Gilead Sciences, Inc., Actelion Pharmaceuticals Ltd. and United Therapeutics Corporation are pursuing the development or are currently marketing pharmaceuticals that target VEGF, HGF, ErbB3, Notch 3 or other pathways on which we may focus, as well as cachexia. It is probable that the number of companies seeking to develop competing products and therapies will increase.

Many of our competitors, either alone or with their strategic partners, have greater financial, technical and human resources than we do and greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products, and the commercialization of those products. Many are already marketing products to treat the same indications, and having the same biological targets, as the product candidates we are developing, including with respect to renal cell carcinoma. In addition, many of these competitors have significantly greater commercial infrastructures than we have. We will not be able to compete successfully unless we effectively:

- design and develop products that are superior to other products in the market in terms of, among other things, both safety and efficacy;
- obtain patent and/or other proprietary protection for our processes and product candidates;
- obtain required regulatory approvals;
- obtain favorable reimbursement, formulary and guideline status; and
- collaborate with others in the design, development and commercialization of new products.

Established competitors may invest heavily to quickly discover and develop novel compounds that could make our product candidates obsolete. 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. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

There are currently 11 FDA-approved drugs in oncology which, like tivozanib, target the VEGF pathway as a part or all of their inhibitory mechanism. Eight of the FDA-approved VEGF pathway inhibitors are oral small molecule

receptor tyrosine kinase inhibitors, or TKIs. Many of the approved VEGF pathway inhibitor agents are in ongoing development in additional cancer indications including RCC. Additionally, we are aware of a number of companies that have ongoing programs to develop both small molecules and biologics that target the VEGF pathway. In addition, the emergence of PD1/PDL1 inhibitor therapies present additional competition for tivozanib in advanced RCC. Additional clinical trials for mono and combination therapies of PD1/PDL1 with VEGF TKIs are in the pipeline targeting RCC.

We believe the products that are considered competitive with ficlatuzumab include those agents targeting the HGF/c-Met pathway. We believe the most direct competitors to our AV-203 program are monoclonal antibodies that specifically target the ErbB3 receptor. There are also other agents that target ErbB3 as a part or all of their inhibitory mechanism. Only a limited number of agents have been approved for the treatment or prevention of cachexia caused by any disease. However, a number of agents with different mechanisms of action have completed or are currently being studied in phase 2 trials in cachexia or muscle wasting. There are no currently approved Notch 3 inhibitors, although there is at least one Notch 3 inhibitor currently in clinical trials. There are multiple treatments approved for pulmonary arterial hypertension through various mechanisms.

Even if we, or any collaborators, are able to commercialize any product candidate that we, or they, develop, the product 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. If coverage is not available, or reimbursement is limited, we, or any collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their 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 a time consuming and costly process that 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 applied consistently or obtained in the first instance.

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 any 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 or the ability of any collaborators 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 commercialize successfully 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 or that of any collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost effective, and coverage and reimbursement may not be available to our customers, or those of any collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost control initiatives could cause us, or any collaborators, to decrease the price we, or they, 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, and coverage may be more limited than the indications 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, by way of 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. 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, or any collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot

successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense could require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

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

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical studies in the amount of $20 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Risks Related to Our Dependence on Third Parties

We rely on third parties, such as clinical research organizations, or 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 have relied, and will rely, on contract research organizations and other third parties to assist us in managing, monitoring and otherwise carrying out many of these trials. We compete with larger companies for the resources of these third parties.

Although we plan to continue to rely on these third parties to conduct our ongoing 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, commonly referred to as good clinical practices, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements.

The third parties on whom we rely generally may terminate their engagements with us at any time. If we are required to enter into alternative arrangements because of any such termination, the introduction of our product candidates to market could be delayed.

If these third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our clinical trial protocols or regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may not meet regulatory requirements. If our clinical trials do not meet regulatory requirements or if

these third parties need to be replaced, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates and our reputation could be harmed.

We rely on third-party manufacturers to produce our preclinical and clinical product candidate supplies and we intend to rely on third parties to produce commercial supplies of any approved product candidates. Any failure by a third-party manufacturer to produce supplies for us may delay or impair our ability to complete our clinical trials or commercialize our product candidates.

We do not possess all of the capabilities to fully commercialize any of our product candidates on our own. 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 other product candidates or 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 and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications), 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 cGMP and similar foreign standards. Any failure by our third-party manufacturers to comply with cGMP or failure to scale-up manufacturing processes as needed, including any failure to 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. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our product candidates. Such suppliers may not sell this capital equipment or these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of this capital equipment or these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

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 in quantities or in a timely manner necessary to develop and commercialize related products. If we successfully commercialize any of our drugs, we may be required to establish or access large-scale commercial manufacturing capabilities. In addition, as our drug development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. 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 in the event that one or more of our product candidates gains marketing approval, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers.

If any of our current or future strategic partners fails to perform its obligations or terminates its agreement with us, the development and commercialization of the product candidates under such agreement could be delayed or terminated

and our business could be substantially harmed.

As part of our business strategy, we have entered into strategic partnerships for each of our development programs, and we plan to enter into additional strategic partnerships in the future. If any current or future strategic partners do not devote sufficient time and resources to its arrangements with us, we may not realize the potential commercial benefits of the arrangement, and our results of operations may be adversely affected. In addition, 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 its own, and we may find it difficult to attract a new alliance partner for such product candidate. For example, Biodesix can opt-out of its agreement with us after the completion of the proof of concept trial prior to the first commercial sale of ficlatuzumab, at which point Biodesix would not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical studies.

Much of the potential revenue from any of our strategic partnerships will likely consist of contingent payments, such as 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 because of 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.

For example, Pharmstandard has recently informed us that, based on adverse economic and financial conditions in Russia, they are seeking to renegotiate their obligation to make milestone payments to us under their license agreement with us. If one or more of our strategic partners fails to develop or effectively commercialize product candidates for any of the foregoing reasons, we may not be able to replace the strategic partner with another partner to develop and commercialize a product candidate under the terms of the strategic partnership. We may also be unable to obtain, on terms acceptable to us, a license from such strategic partner to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

Risks Related to Our Intellectual Property Rights

We could be unsuccessful in obtaining adequate patent protection for one or more of our product candidates, 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 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. The scope of patent protection that the U.S. Patent and Trademark Office will grant with respect to the antibodies in our antibody product pipeline is uncertain. It is possible that the U.S. Patent and Trademark Office 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.

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 corporate 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. 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 United States Patent and Trademark Officer, 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 U.S. Patent and Trademark Office, 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 United States Patent and Trademark Office and the European Patent Office. Although we have conducted due diligence on patents we have exclusively in-licensed, and we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability,

we would lose at least part, and perhaps all, of the patent protection on one of our products. Such a loss of patent protection could have a material adverse impact on our business.

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

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

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

With regard to tivozanib, we are aware of a third-party United States patent, and corresponding foreign counterparts, that contain broad claims related to use of an organic compound, that, among other things, inhibits the tyrosine phosphorylation of a VEGF receptor caused by VEGF binding to such VEGF receptor. We are also aware of third-party United States patents that contain broad claims related to the use of a tyrosine kinase inhibitor in combination with a DNA damaging agent such as chemotherapy or radiation and we have received written notice from the owners of such patents indicating that they believe we may need a license from them in order to avoid infringing their patents. With regard to ficlatuzumab, we are aware of two separate families of United States patents, United States patent applications and foreign counterparts, with each of the two families being owned by a different third-party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. With regard to AV-203, we are aware of a third-party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Additionally, we are aware of a United States patent application and foreign counterparts that contains claims to the use of a companion diagnostic in conjunction with AV-203. Based on our analyses, if any of the above third-party patents were asserted against us, we do not believe our proposed products or activities would be found to infringe any valid claim of these patents. 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 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 product(s). 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, continue our internal research programs, in-license needed technology, or enter into strategic partnerships that would help us bring our product candidates to market.

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

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

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

AV-380 and tivozanib 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 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 used in our AV-380 program, and from KHK for tivozanib. 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 under which we are licensed and on which our business depends. 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, including Novartis and Pharmstandard, 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 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 field of oncology. 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 vendors of laboratory or clinical development services or potential strategic partners. In addition, each of our employees is 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 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, contractors, 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.

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

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

- Others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
    - Issued patents that we own or have exclusively licensed may not provide us with a competitive advantage; for example, our issued patents may not be broad enough to prevent the commercialization of competitive antibodies that are biosimilar to one or more of our antibody products, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.
- We may not develop additional proprietary technologies that are patentable.
- 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 biopharma industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharma patents is costly, time-consuming and inherently uncertain. In addition, several recent events 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. The new patent law introduces changes including a first-to-file system for determining which inventors may be entitled to receive patents, and a new post-grant review process that allows third parties to challenge newly issued patents. It remains to be seen how the biopharma industry will be affected by such changes in the patent system. In addition, the 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 U.S. Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that could 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

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

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export

and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the European Medicines Agency 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 and our collaborators have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

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. Securing regulatory approval 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 preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. 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. 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. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions.

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

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

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We, or any future collaborators, may seek orphan drug designations for other product candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. 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.

Even if we, or any future collaborators, obtain 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. 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, more effective or makes a major contribution to patient care.

Even if we, or any current or future collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any current or future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing 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 and any current or future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any current or future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any current or future collaborators, receive marketing approval for one or more of our product candidates, we, and any current or future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any current or future collaborators, are not able to comply with post-approval regulatory requirements, we, and any current or future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any current or future collaborators', ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we or our collaborators obtain marketing approval 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 or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Any product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, 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.

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. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. 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.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or 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 any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

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

Our relationships with healthcare providers, physicians and third party payors will be 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 any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, 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, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes 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, currently set at $5,500 to $11,000 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
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HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers.

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 may require product 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 preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our other product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, 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 any approved products.

For example, 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 PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following:

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an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent product labeling and post-marketing testing and other requirements.

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, 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 Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

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

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

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

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

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the European Union, 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 any current or future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

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.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data 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 public disclosure of confidential or proprietary information, we could incur liability and our product development and commercialization efforts could be delayed.

Risks Related to Employee Matters and Managing 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 reduction in force related to the restructuring we completed this year could make it more difficult to retain or attract employees in the future. The loss of services of employees, and in particular, of a member of management could delay or prevent our ability to successfully maintain or enter into new licensing arrangements or collaborations, the successful development of our product candidates, the completion of our planned clinical trials or the commercialization of our product candidates. We do not carry “key person” insurance covering any members of our senior management. Our employment arrangements with all of these individuals are “at will,” meaning they or we can terminate their service at any time.

We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to reward qualified individuals than we do. We may face challenges in retaining our existing senior management and key employees and recruiting new employees to join our company as our business needs change. 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 may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees 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, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee 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 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 and employees 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 or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee 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

If we fail to meet the requirements for continued listing on the NASDAQ Global Select 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 for quotation on the NASDAQ Global Select Market. We are required to meet specified requirements in order to maintain our listing on the NASDAQ Global Select Market, including, among other things, a minimum bid price of $1.00 per share. Our bid price has recently fallen below $1.00 from time to time. If our bid price falls below $1.00 per share for 30 consecutive business days, we will receive a deficiency notice from NASDAQ advising us that we have 180 days to regain compliance by maintaining a minimum bid price of at least $1.00 for a minimum of ten consecutive business days. Under certain circumstances, NASDAQ could require that the minimum bid price exceed $1.00 for more than ten consecutive days before determining that a company complies.

If we fail to satisfy the NASDAQ Global Select Market's continued listing requirements, we may transfer to the NASDAQ Capital Market, which generally has lower financial requirements for initial listing, to avoid delisting, or, if we fail to meet its listing requirements, the OTC Bulletin Board A transfer of our listing to the NASDAQ Capital Market or 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.

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:

- new products, product candidates or new uses for existing products introduced or announced by our strategic partners, or our competitors, and the timing of these introductions or announcements;
- actual or anticipated results from and any delays in our clinical trials;
- results of regulatory reviews relating to our product candidates;
- the results of our efforts to discover, 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 and/or operations;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;
- general economic 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; and
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

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, since our May 2, 2013 announcement regarding the vote of the Oncologic Drugs Advisory Committee of the FDA, we and certain of our former officers and directors have been involved in a number of legal proceedings, including those described below under the heading "Legal Proceedings" in Part II—Item 1 of this Form 10-Q. These proceedings and other similar litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

We may not achieve development and commercialization goals in the time frames that we publicly estimate, 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 the initiation and completion of clinical trials, filing and approval of regulatory applications for our product candidates and other developments and milestones under our research and development programs. The actual timing of these events can vary significantly due to a number of factors, including, without limitation, delays or failures in our and our current and potential collaborators' preclinical studies or clinical trials, the amount of time, effort and resources committed to our programs by us and our current and potential collaborators and the uncertainties inherent in the regulatory approval process. As a result, there can be no assurance that our or our current and potential collaborators' preclinical studies and clinical trials will advance or be completed in the time frames we expect or announce, that we or our current and potential collaborators will make regulatory submissions or receive regulatory approvals as planned or that we or our current and potential collaborators will be able to adhere to our current schedule for the achievement

of key milestones under any of our programs. If we or any collaborators fail to achieve one or more of the milestones described above as planned, our business could be materially adversely affected and the price of our common stock could decline.

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

Our management has broad discretion on where and how to use our cash and cash equivalents and you will be relying on the judgment of our management regarding the application of our available cash and cash equivalents to fund our operations. Our management might not apply our cash or 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.

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 status of our clinical development programs;
- the level of expenses incurred in connection with our clinical development programs, including development and manufacturing costs relating to our clinical development candidates;
- any intellectual property infringement lawsuit or other litigation in which we may become involved;
- the implementation of our current restructuring and cost-savings strategies;
- the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement;
- costs associated with lawsuits against us, including the current purported class action and derivative lawsuits described elsewhere in this report under “Part II, Item 1—Legal Proceedings;”
- changes in our loan agreement with Hercules, including the existence of any event of default that may accelerate payments due thereunder; 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.

As widely reported, global credit and financial markets have been experiencing extreme volatility, and in some cases, disruptions, over the past several years, in many cases, over extended periods. Although certain of these trends have recently showed signs of reversing, there can be no assurance that rapid or extended periods of deterioration in credit and financial markets and confidence in economic conditions will not occur. 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.

At June 30, 2016, we had $39.5 million of cash, cash equivalents and marketable securities consisting of cash on deposit with banks, money market funds, U.S. government agency securities, and corporate debt securities, including commercial paper. 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. 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 or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents owned by us.

There is a possibility that our stock price may decline because of volatility of the stock market and general economic conditions.

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 event 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.

A decline in our stock price may affect future fundraising efforts.

We currently have no product revenues, and depend entirely on funds raised through other sources. One source of such funding is future debt and/or equity offerings. Our ability to raise funds in this manner depends upon, among other things, our stock price, which may be affected by capital market forces, evaluation of our stock by securities analysts, product development success (or failure), and internal management operations and controls.

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 shareholders.

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 shareholders 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 as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

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

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls, and requires our independent registered public accounting firm to attest to the effectiveness of our internal controls. Despite our efforts, we can provide no assurance as to our, or our independent registered public accounting firm's, conclusions with respect to the effectiveness of our internal control over financial reporting under Section 404. There is a risk that neither we nor our independent registered public accounting firm will be able to continue 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.

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

You 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. 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.

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, 2015, we had federal and state net operating loss carryforwards of $444.5 million and $338.7 million, respectively, and federal and state research and development tax credit carryforwards of $10.1 million and $4.0 million, respectively, each of which if not utilized will expire at various dates through 2035. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, 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 carryforwards and other pre change tax attributes to offset its post change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of

which may be outside of our control. We have not conducted a detailed study to document whether our historical activities qualify to support the research and development credit carryforwards. 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, it would harm our future operating results by effectively increasing our future tax obligations.

Item 6. Exhibits.

The exhibits listed in the Exhibit Index to this Quarterly Report on Form 10-Q are incorporated herein by reference.

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: August 4, 2016 By: /s/ Keith S. Ehrlich
Keith S. Ehrlich, C.P.A.
Chief Financial Officer and Principal Financial and Accounting Officer

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.1	Securities Purchase Agreement, dated May 13, 2016, by and among the Company and the Investors named therein	8-K	001-34655	05/13/2016	10.1	
10.2	Form of Warrant to Purchase Common Stock	8-K	001-34655	05/13/2016	10.2	
10.3	Registration Rights Agreement, dated May 13, 2016, by and among the Company and the Investors named therein	8-K	001-34655	05/13/2016	10.3	
10.4	Amendment No. 4 to Loan and Security Agreement, dated May 13, 2016, by and among the Company and the Lenders party thereto					X
10.5	Warrant Agreement, dated May 13, 2016, by and between the Company and Hercules Capital, Inc.	8-K	001-34655	05/13/2016	10.5	
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document.					X

101.SCH	XBRL Taxonomy Extension Schema Document.	X
101.CAL	XBRL Taxonomy Calculation Linkbase Document.	X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.	X
101.LAB	XBRL Taxonomy Label Linkbase Document.	X
101.PRE	XBRL Taxonomy Presentation Linkbase Document.	X