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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2015

or

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

For the transition period from _____ to _____

Commission File Number: 001-36579

Avalanche Biotechnologies, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**20-5258327**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

1035 O'Brien Drive, Suite A
Menlo Park, CA
(Address of principal executive offices)

94025
(Zip Code)

(650) 272-6269
(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 ☒ 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 ☒ 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 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	☐
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 ☒

As of April 30, 2015 there were 25,528,922 shares of the registrant's common stock, par value $0.0001 per share, outstanding.

Avalanche Biotechnologies, Inc.

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PART I—FINANCIAL INFORMATION

Item 1. Unaudited Condensed Consolidated Financial Statements

Avalanche Biotechnologies, Inc.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands except share and per share data)

	March 31, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$201,849	$ 159,404
Marketable securities	88,276	—
Prepaid expenses and other current assets	1,007	874
Total current assets	291,132	160,278
Property and equipment, net	1,421	1,085
Deposit and other long-term assets	138	543
Total assets	$292,691	$ 161,906
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,787	$ 951
Accrued expenses and other current liabilities	2,528	3,707
Deferred revenue	2,313	813
Total current liabilities	7,628	5,471
Long-term liabilities:		
Deferred rent	440	306
Deferred revenue, net of current portion	4,943	6,646
Total liabilities	13,011	12,423
Commitments and contingencies (Note 8)		
Stockholders' equity		
Preferred stock, $0.0001 par value, 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.0001 par value, 300,000,000 shares authorized at March 31, 2015 and December 31, 2014; 25,473,938 and 22,754,037 shares issued and outstanding at March 31, 2015 and December 31, 2014, respectively	3	2
Additional paid-in-capital	325,934	186,186
Accumulated other comprehensive (loss) income	(33)	10
Accumulated deficit	(46,224)	(36,715)
Total stockholders' equity	279,680	149,483
Total liabilities and stockholders' equity	$292,691	$ 161,906

See accompanying notes to condensed consolidated financial statements

Avalanche Biotechnologies, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(In thousands except per share data)

	Three Months Ended March 31,	
	2015	2014
Collaboration and license revenue	$ 203	$ 30
Operating expenses:		
Research and development	5,621	910
General and administrative	4,143	726
Total operating expenses	9,764	1,636
Operating loss	(9,561)	(1,606)
Other income (expense):		
Interest expense	—	(14)
Other income (expense), net	52	(6)
Changes in fair value of warrant liabilities	—	(37)
Total other income (expense), net	52	(57)
Net loss	$ (9,509)	$ (1,663)
Other comprehensive loss:		
Net unrealized loss on marketable securities	(35)	—
Foreign currency translation adjustment	(8)	—
Comprehensive loss	$ (9,552)	$ (1,663)
Net loss per share attributable to common stockholders-basic and diluted	$ (0.38)	$ (0.45)
Weighted-average common shares outstanding-basic and diluted	24,887	3,673

See accompanying notes to condensed consolidated financial statements

Avalanche Biotechnologies, Inc.
Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2015	**2014**
Cash flows from operating activities:		
Net loss	$ (9,509)	$(1,663)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	118	9
Stock-based compensation expense	773	115
Non-cash interest expense	—	14
Amortization of premium on marketable securities	59	—
Change in fair value of warrant liabilities	—	37
Change in operating assets and liabilities:		
Accounts receivable	—	(225)
Prepaid expenses and other assets	(120)	(150)
Deposit	(1)	—
Accounts payable	1,771	178
Accrued expenses and other liabilities	(764)	269
Deferred revenue	(203)	—
Deferred rent	134	69
Net cash used in operating activities	(7,742)	(1,347)
Cash flows from investing activities:		
Purchases of marketable securities	(88,370)	—
Purchases of property and equipment	(411)	(47)
Net cash used in investing activities	(88,781)	(47)
Cash flows from financing activities:		
Proceeds from sales of common stock, net of offering costs	138,954	—
Proceeds from issuance of convertible notes	—	1,000
Proceeds from issuance of common stock pursuant to options exercises	21	—
Net cash provided by financing activities	138,975	1,000
Effect of foreign currency exchange rate on cash	(7)	(1)
NET INCREASE (DECREASE) IN CASH	42,445	(395)
Cash and cash equivalents at beginning of period	159,404	564
Cash and cash equivalents at end of period	$201,849	$ 169
Supplemental disclosures of cash flow information		
Cash paid for interest	$ —	$ 5
Supplemental disclosures of noncash investing and financing information		
Warrants issued in connection with license agreements	$ —	$ 41
Fixed assets in accounts payable and accrued liabilities	$ 278	$ —
Deferred initial public offering expenses in accounts payable	$ —	$ 46

See accompanying notes to condensed consolidated financial statements.

Avalanche Biotechnologies, Inc.
March 31, 2015

Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Organization and Basis of Presentation

Avalanche Biotechnologies, Inc. (the "Company", "we" or "us") was incorporated in Delaware on July 17, 2006, and is headquartered in Menlo Park, California. The Company is a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. Since the Company's inception, it has devoted its efforts principally to performing research and development activities, including early clinical trials, filing patent applications, obtaining regulatory approvals, hiring personnel, and raising capital to support these activities.

The Company has not generated any revenue from the sale of products since its inception. The Company has experienced net losses since its inception and has an accumulated deficit of $46.2 million as of March 31, 2015. The Company expects to incur losses and have negative net cash flows from operating activities as it expands its portfolio and engages in further research and development activities, particularly conducting preclinical studies and clinical trials.

Follow-on Offering—In January 2015, the Company completed a public offering of 2,369,375 shares of its common stock (Follow-on Offering), which included 359,918 shares the Company issued pursuant to the underwriters' exercise of their option to purchase additional shares, and the Company received net proceeds of approximately $130.6 million, after underwriting discounts, commissions and offering expenses.

In March 2015, (i) the Company received net proceeds of approximately $8.3 million, after discounts and other issuance costs, which resulted from the sale of 230,000 common shares, and (ii) the Company issued 230,000 common shares to a shareholder that exercised warrants prior to the initial public offering.

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) and following the requirements of the Securities and Exchange Commission (SEC) for interim reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by U.S. GAAP can be condensed or omitted. These condensed consolidated financial statements have been prepared on the same basis as the Company's annual consolidated financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, which are necessary for a fair statement of the Company's financial information. The results of operations for the three month period ended March 31, 2015 are not necessarily indicative of the results to be expected for the full year or any other future period. The balance sheet as of December 31, 2014 has been derived from audited consolidated financial statements at that date but does not include all of the information required by U.S. GAAP for complete financial statements.

The accompanying condensed consolidated financial statements and related financial information should be read in conjunction with the audited consolidated financial statements and the related notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC.

2. Summary of Significant Accounting Policies

The accounting policies followed in the preparation of the interim condensed consolidated financial statements are consistent in all material respects with those presented in Note 2 to the consolidated financial statements included in the Company's Annual Report on Form 10-K for the year ended December 31, 2014.

Reclassifications—The Company has reclassified certain prior period amounts to conform to the current period presentation. The Company reclassified changes in fair value of warrant liabilities from other income (expense), net and presented it as a separate line item on the condensed consolidated statements of operations and comprehensive loss. The reclassification had no impact on the total income (expense), net or net loss.

Cash and Cash Equivalents—The Company considers all highly liquid investments purchased with original maturities of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents include cash held in banks and money market accounts. Cash equivalents are stated at fair value.

Marketable Securities—All marketable securities, which consist of debt securities and certificates of deposit, have been classified as "available for sale" and are carried at fair value. Unrealized gains and losses, net of any related tax effects, are excluded from earnings and are included in other comprehensive loss and reported as a separate component of stockholders' equity until realized. Realized gains and losses and declines in value judged to be other than temporary, if any, on available-for-sale securities are included in other income (expense), net. The cost of securities sold is based on the specific-identification method. The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Interest on short-term investments is included in interest income. In accordance with the Company's investment policy, management invests to diversify credit risk and only invests in securities with high credit quality, including U.S. government securities.

The Company regularly evaluates whether declines in the fair value of its investments below their cost are other than temporary. The evaluation includes consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities, and whether it is more likely than not that the Company will be required to sell the securities before the recovery of their amortized cost basis. If the Company determines that the decline in fair value of an investment is below its accounting basis and this decline is other than temporary, the Company would reduce the carrying value of the security it holds and records a loss for the amount of such decline. The Company has not recorded any realized losses or declines in value judged to be other than temporary on its investments.

Recently Issued Accounting Pronouncements—In August 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standard Update (ASU) 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, requiring management to evaluate whether events or conditions could impact an entity's ability to continue as a going concern and to provide disclosures if necessary. Management will be required to perform the evaluation within one year after the date that the financial statements are issued. Disclosures will be required if conditions give rise to substantial doubt and the type of disclosure will be determined based on whether management's plans will be able to alleviate the substantial doubt. The accounting standards update will be effective for the first annual period ending after December 15, 2016, and for annual periods and interim periods thereafter with early application permitted. The adoption of this guidance is not expected to impact the Company's financial position or results of operations.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in ASC 605*, Revenue Recognition*. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. On April 1, 2015, FASB voted to propose to defer the effective date of this ASU by one year to December 15, 2017. The ASU's effective date for the Company will be January 1, 2018. The Company is evaluating the application of this ASU, but has not yet determined the potential effects it may have on the Company's consolidated financial statements.

3. Cash Equivalents and Marketable Securities

The following is a summary of the cash equivalents and marketable securities:

(in thousands)	MARCH 31, 2015			
	AMORTIZED COST BASIS	UNREALIZED GAINS	UNREALIZED LOSSES	ESTIMATED FAIR VALUE
Money Market Funds	$ 174,588	$ —	$ —	$ 174,588
Certificates of Deposit	7,680	—	(4)	7,676
U.S. Treasury Securities	25,436	—	(6)	25,430
U.S. Government Agency Securities	62,094	1	(26)	62,069
	269,798	1	(36)	269,763
Less: cash equivalents	(181,487)	—	—	(181,487)
Total marketable securities	$ 88,311	$ 1	$ (36)	$ 88,276

The Company did not hold any available-for-sale securities as of December 31, 2014. As of March 31, 2015, the contractual maturities of the Company's marketable securities were less than one year. Management determined that the gross unrealized losses of $36,000 on the Company's marketable securities as of March 31, 2015 were temporary in nature. The Company currently does not intend to sell these securities prior to maturity and does not consider these investments to be other-than-temporarily impaired at March 31, 2015. There were no sales of available-for-sale securities in any of the periods presented.

4. Fair Value Measurements and Fair Value of Financial Instruments

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

The fair value of Level 1 securities are determined using quoted prices in active markets for identical assets. Level 1 securities consist of highly liquid money market funds. Financial assets and liabilities are considered Level 2 when their fair values are determined using inputs that are observable in the market or can be derived principally from or corroborated by observable market data such as pricing for similar securities, recently executed transactions, cash flow models with yield curves, and benchmark securities. In addition, Level 2 financial instruments are valued using comparisons to like-kind financial instruments and models that use readily observable market data as their basis. U.S. Treasury securities, U.S. government agency securities and certificate of deposit are valued primarily using market prices of comparable securities, bid/ask quotes, interest rate yields and prepayment spreads and are included in Level 2.

The Company's financial instruments had consisted of Level 3 liabilities. In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3 within the valuation hierarchy. Level 3 liabilities that were measured at estimated fair value on a recurring basis consisted of common and preferred stock warrant liabilities.

The estimated fair values of the outstanding common and preferred stock warrant liabilities are measured using the Black-Scholes valuation model. This method of valuation involves using such inputs as the estimated fair value of the underlying stock at the measurement date, the expected term, which is the remaining contractual term of the warrants, risk-free interest rates, expected dividends on stock and expected volatility of the price of the underlying stock. Due to the nature of these inputs, the valuation of the warrants is considered a Level 3 measurement. The convertible preferred stock and common stock warrant liabilities will increase or decrease each period based on the fluctuations of the fair value of the underlying security. A significant fluctuation in the common or convertible preferred stock fair value would result in a material change in the fair values of the convertible preferred stock and common stock warrant liabilities.

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at estimated fair value using Level 3 inputs. There were no transfers within the hierarchy during the year ended December 31, 2014 and the three months ended March 31, 2015. As of December 31, 2014 and March 31, 2015, the Company had no Level 3 assets or liabilities.

The following table summarizes, for assets recorded at fair value, the respective fair value and the classification by level of input within the fair value hierarchy as described above (in thousands):

	TOTAL CARRYING VALUE	QUOTED PRICES IN ACTIVE MARKETS (LEVEL 1)	SIGNIFICANT OTHER OBSERVABLE INPUTS (LEVEL 2)	SIGNIFICANT UNOBSERVABLE INPUTS (LEVEL 3)
March 31, 2015				
Assets:				
Money market funds	$ 174,588	$ 174,588	$ —	$ —
Certificates of deposit	7,676	—	7,676	—
U.S. Treasury securities	25,430	—	25,430	—
U.S. government agency securities	62,069	—	62,069	—
Total cash equivalents and marketable securities	$ 269,763	$ 174,588	$ 95,175	$ —
December 31, 2014				
Assets:				
Money market funds	$ 40,000	$ 40,000	$ —	$ —
Total cash equivalents	$ 40,000	$ 40,000	$ —	$ —

The following table provides a summary of changes in the estimated fair value of the Company's warrants liabilities and embedded derivative liability measured at estimated fair value using significant Level 3 inputs (in thousands):

	CONVERTIBLE PREFERRED STOCK WARRANT LIABILITY (1)	COMMON STOCK WARRANT LIABILITY (2)
Balance—January 1, 2014	91	42
Issuance of common stock warrant	—	(41)
Change in fair value	38	(1)
Balance—March 31, 2014	$ 129	$ —

(1) In July 2014, all of the outstanding warrants to purchase convertible preferred stock and common stock were exercised immediately prior to the completion of the initial public offering (IPO).
(2) In March 2014, the common stock warrant was issued and was recorded to additional paid-in capital.

The fair value of the warrants to purchase convertible preferred stock was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of $3.74 per share, contractual term of the warrants of 1.44 years, a risk-free interest rate of 0.1%, an expected volatility of 59% and a 0% expected dividend yield.

5. Significant Agreements

University of California—In May 2010, the Company entered into a license agreement, as amended, with the Regents of the University of California (Regents) for exclusive rights in the U.S. to certain patents owned by the Regents. Under the terms of the agreement, the Company paid an upfront license fee of $100,000 and agreed to reimburse the Regents for patent-related expenses. The Company is obligated to pay the Regents royalties on net sales, if any, as well as an annual maintenance fee of $50,000 beginning in the calendar year after the first commercial sale of a licensed product and milestone payments related to the achievement of certain clinical and regulatory goals totaling up to $900,000 for the first indication and $500,000 for each additional indication for up to two additional indications. Through March 31, 2015, none of these goals had been achieved, and no milestones were payable.

6. Property and Equipment, Net

Property and equipment, net consists of the following (in thousands):

	March 31, 2015	December 31, 2014
Computer equipment and software	$ 182	$ 142
Laboratory equipment	1,420	1,012
Furniture and fixtures	83	73
Leasehold improvements	44	48
Total property and equipment	1,729	1,275
Less accumulated depreciation and amortization	(308)	(190)
Property and equipment, net	$ 1,421	$ 1,085

Depreciation and amortization expense related to property and equipment for the three months ended March 31, 2015 and 2014 was $118,000 and $9,000, respectively.

7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following (in thousands):

	March 31, 2015	December 31, 2014
Employee compensation	$ 888	$ 1,509
Accrued professional fees	1,185	1,236
Accrued clinical and process development costs	412	942
Other	43	20
Total accrued expenses and other current liabilities	$ 2,528	$ 3,707

8. Commitments and Contingencies

Collaborations and License Agreements

The Company is a party to various agreements, principally relating to licensed technology that requires future payments relating to milestones or royalties on future sales of specified products. Through March 31, 2015, none of the goals had been achieved under the license agreements and no cash milestones were accrued or payable. Because the achievement of these milestones is not fixed and determinable, such commitments have not been included in the Company's consolidated balance sheets.

Guarantees and Indemnifications

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for indemnification for certain liabilities. The exposure under these agreements is unknown because it involves claims that may be made against the Company in the future but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations. The Company also has indemnification obligations to its directors and executive officers for specified events or occurrences, subject to some limits, while they are serving at the Company's request in such capacities. There have been no claims to date and the Company believes the fair value of these indemnification agreements is minimal. Accordingly, the Company has not recorded any liabilities for these agreements as of March 31, 2015.

9. Related-Party Convertible Notes

On October 22, 2013, the Company entered into a convertible note purchase agreement with a related party investor for the issuance and sale of up to an aggregate principal amount of $5.0 million of convertible notes (2013 Notes). In each of January 2014 and April 2014, the Company borrowed an aggregate principal amount of $1.0 million of 2013 Notes.

The difference between the fair value of the securities into which the debt was convertible and the effective conversion price on the borrowing date represents a beneficial conversion feature. In connection with the January 2014 and April 2014 borrowings, the Company recorded the fair value of the beneficial conversion feature of $1.0 million and $1.0 million, respectively, by allocating a portion of the proceeds to additional paid-in capital, resulting in a discount on the convertible instrument, to be amortized over the repayment period using the effective interest method. The 2013 Notes were converted to 295,115 shares of Series B convertible preferred stock in April 2014.

At December 31, 2014 and March 31, 2015, there are no outstanding convertible notes recorded in our condensed consolidated balance sheets.

10. Stock Option Plans

On December 26, 2006, the Company adopted the 2006 Equity Incentive Plan, which was amended by the board of directors on November 15, 2012 (2006 Plan). The 2006 Plan allowed for the granting of ISOs and NSOs to the employees, members of the board of directors and consultants of the Company. ISOs were granted only to the Company's employees, including officers and directors who are also employees. NSOs were granted to the employees and consultants. In July 2014, the Company's board of directors and its stockholders approved the establishment of the 2014 Equity Incentive Award Plan (2014 Plan), effective upon the date upon which the registration statement for the IPO was declared effective, which was July 30, 2014. As of the date of the IPO, the Company reserved for issuance under the 2014 Plan a total of 2,088,332 shares of its common stock, plus any additional shares that would otherwise return to the 2006 Plan as a result of forfeiture, termination or expiration of awards previously granted under the 2006 Plan. Options may no longer be issued under the 2006 Plan after July 30, 2014, the effective date of the 2014 Plan. In addition, the 2014 Plan provides for annual increases in the number of shares available for issuance thereunder on the first business day of each fiscal year, beginning with 2015, equal to four percent (4%) of the number of shares of the Company's common stock outstanding as of such date or a lesser number of shares as determined by the Company's board of directors.

As of March 31, 2015, a total of 8,454,368 shares of common stock were authorized for issuance and 2,812,326 shares were available for future grants under the 2014 Plan.

Options under the 2014 Plan may be granted for periods of up to 10 years and at prices no less than 100% of the estimated fair value of the shares on the date of grant as determined by the board of directors, provided, however, that the exercise price of an ISO and NSO granted to a 10% shareholder may not be less than 110% of the estimated fair value of the shares on the date of grant. Options granted to employees and non-employees generally vest ratably over four years.

In July 2014, the Company's board of directors and its stockholders approved the establishment of the 2014 Employee Stock Purchase Plan (2014 ESPP). The Company reserved for issuance 208,833 shares of its common stock and provided for annual increases in the number of shares available for issuance on the first business day of each fiscal year, beginning in 2015, equal to the lesser of one percent (1%) of the number of shares of the Company's common stock outstanding as of such date or a number of shares as determined by the Company's board of directors. During 2015, no shares were issued under the 2014 ESPP. A total of 436,373 shares of common stock have been reserved for issuance under the 2014 ESPP and were available for issuance under the 2014 ESPP as of March 31, 2015.

The following table summarizes option activity under our stock plans and related information:

	NUMBER OF SHARES	WEIGHTED-AVERAGE EXERCISE PRICE	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	AGGREGATE INTRINSIC VALUE (a) (IN THOUSANDS)
Balances, January 1, 2015	4,931,858	$ 5.61	8.2	$ 238,653
Options granted	142,750	$ 50.15		
Options exercised	(120,526)	$ 0.26		
Options cancelled	(1,200)	$ 11.50		
Balances, March 31, 2015	4,952,882	$ 7.03	7.9	$ 165,855
Vested and expected to vest as of March 31, 2015	4,910,656	$ 6.97	7.9	$ 164,768
Exercisable as of March 31, 2015	1,998,130	$ 0.53	7.0	$ 79,984

(a) The aggregate intrinsic value is calculated as the difference between the option exercise price and the closing price of common stock of $40.52 per share as of March 31, 2015.

The weighted-average fair values of options granted during the three months ended March 31, 2015 and 2014 were $34.00 and $1.93, respectively. The total intrinsic value of options exercised during the three months ended March 31, 2015 was $4.4 million. There were no options exercised during the three months ended March 31, 2014.

The following table summarizes information with respect to stock options outstanding and currently exercisable and vested.

As of March 31, 2015:

	OPTIONS OUTSTANDING		OPTIONS EXERCISABLE AND VESTED	
RANGE OF EXERCISE PRICES	NUMBER OUTSTANDING	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	NUMBER OUTSTANDING	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)
$ .0001 – $0.27	2,961,075	7.0	1,853,993	6.8
$ 0.28 – $2.95	473,757	8.9	136,845	8.8
$ 2.96 – $9.16	265,000	9.1	—	—
$ 9.17 – $11.50	277,200	9.3	—	—
$ 11.51 – $35.00	769,850	9.4	—	—
$ 35.01 – $58.92	206,000	9.8	7,292	9.7

The Company has recorded aggregate stock-based compensation expense related to the issuance of stock option awards to employees and nonemployees in the condensed consolidated statement of operations and comprehensive loss as follows (in thousands):

	Three Months Ended March 31,	
	2015	2014
Research and development	$ 284	$ 69
General and administrative	489	46
Total share-based compensation	$ 773	$ 115

Stock Options Granted to Employees

The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	Three Months Ended March 31,	
	2015	2014
Option grants:		
Expected volatility	78%	78%
Expected term (in years)	6.1	6.0
Expected dividend yield	—	—
Risk-free interest rate	1.8%	1.8%

As of March 31, 2015, there was $18.6 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 3.3 years.

Stock Options Granted to Non-Employees

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The Company believes that the estimated fair value of the stock options is more readily measurable than the fair value of the services rendered. The following weighted-average assumptions were used in estimating non-employees' stock-based compensation expenses:

	Three Months Ended March 31,	
	2015	2014
Option grants:		
Expected volatility	80%	77%
Contractual term remaining (in years)	7.7	7.8
Expected dividend yield	—	—
Risk-free interest rate	1.7%	2.6%

As of March 31, 2015, there was $2.0 million of unrecognized stock-based compensation expense related to non-employees' awards that is expected to be recognized over a weighted-average period of 2.7 years.

Fair Value of Common Stock

In determining the exercise prices for options granted, the Company's board of directors has considered the fair value of the common stock as of each grant date. Prior to the IPO, the fair value of the common stock underlying the stock options was determined by the board of directors at each award grant date based upon a variety of factors, including the results obtained from an independent third party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the current management team, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred shareholders and the prospects of a liquidity event, among others. After the completion of the Company's IPO in August 2014, the fair value of the common stock is based on the closing price of the common stock on the date of grant.

11. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Code. The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. For the three months ended March 31, 2015, the Company contributed $0.1 million to the 401(k) Plan. The amount of contributions that the Company made to the 401(k) Plan during 2014 was $25,000.

12. Net Loss Per Share Attributable to Common Stockholders

The following common stock equivalents outstanding at the end of the period were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect (shares in thousands):

	As of March 31,	
	2015	2014
Options to purchase common stock	4,952	4,134
Warrants to purchase common stock	—	289
Preferred stock	—	3,899
Warrants to purchase preferred stock	—	55
	4,952	8,377

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

The interim financial statements included in this Quarterly Report on Form 10-Q and this Management's Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the financial statements and notes thereto for the year ended December 31, 2014, and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, contained in our Annual Report on Form 10-K, as filed with the U.S. Securities and Exchange Commission (SEC) on March 5, 2015. In addition to historical information, this discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). These forward-looking statements are subject to risks and uncertainties, including those discussed in the section titled "Risk Factors," set forth in Part II – Other Information, Item 1A below and elsewhere in this report that could cause actual results to differ materially from historical results or anticipated results.

Overview

We are a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. We have leveraged our next-generation gene therapy platform, Ocular BioFactory™, to create a robust pipeline of product candidates. Our product candidates are designed to provide long-term efficacy or a functional cure for these diseases by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye.

We are targeting a variety of prevalent and rare genetic ophthalmic diseases with significant unmet medical need. Our lead product candidate is AVA-101 for the treatment of wet age-related macular degeneration (AMD). We believe that this product candidate could transform the treatment paradigm and address the unmet need in the large wet AMD market, which is estimated to be over $6.0 billion worldwide.

We have generated human proof-of-concept data for AVA-101 in a Phase 1 trial with eight wet AMD subjects conducted at Lions Eye Institute (LEI) in Australia. In that Phase 1 trial, AVA-101 was well tolerated with no drug-related adverse events. In addition, subjects treated with AVA-101 showed meaningful improvement in their visual acuity test scores (up to 15 letter improvement on an eye chart from baseline), and most subjects did not receive any rescue injections of standard-of-care therapy (required for subjects exhibiting disease progression) during the one-year trial period. We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. Most adverse events that have been observed to date are mild and not related to AVA-101 or the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015. We own exclusive rights to develop and commercialize AVA-101 worldwide.

In addition to AVA-101, our Ocular BioFactory platform has generated other promising product candidates for the treatment of severe ophthalmic diseases, including AVA-201 and AVA-311. We are developing AVA-201 as a next-generation product candidate for the prevention of wet AMD. AVA-201 produces the same anti-vascular endothelial growth factor (VEGF) protein as AVA-101 using a proprietary, customized delivery mechanism, or vector, that can be administered earlier in the disease progression, before the onset of wet AMD. We own worldwide rights to AVA-201. AVA-311 is being developed in collaboration with our partner Regeneron Pharmaceuticals, Inc. (Regeneron) for the treatment of X-linked retinoschisis (XLRS), a rare genetic disease of the retina with no approved therapy. Based on preclinical studies to date, AVA-311 has been shown to delay the progression of XLRS and improve vision by effectively delivering functional copies of the RS1 gene in retinal cells of mice.

In order to accelerate the pace of generating and developing product candidates for our pipeline, we entered into a broad research collaboration and license agreement with Regeneron in May 2014. Under the terms of the agreement, we intend to jointly discover novel product candidates based on our Ocular BioFactory platform for up to eight therapeutic targets including AVA-311. We have received initial payments of $8.0 million as well as ongoing support for research and development, and we are eligible to receive up to $80.0 million in development and regulatory milestone payments for product candidates directed toward each therapeutic target, for a combined total of up to $640 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single-digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

On January 13, 2015, we completed a public offering of 2,369,375 shares of our common stock (Follow-on Offering), which included 359,918 shares we issued pursuant to the underwriters' exercise of their option to purchase additional shares, and we received net proceeds of approximately $130.6 million, after underwriting discounts, commissions and offering expenses.

In March 2015, (i) the Company received net proceeds of approximately $8.3 million, after discounts and other issuance costs, which resulted from the sale of 230,000 common shares, and (ii) the Company issued 230,000 common shares to a shareholder that exercised warrants prior to the initial public offering.

On March 25, 2015, we announced a new program to develop products based on Avalanche's proprietary Ocular BioFactory™ Platform for the treatment of color vision deficiency, commonly known as red-green color blindness.

Financial Overview

Summary

We have not generated positive cash flow or net income from operations since our inception and, at March 31, 2015, we had an accumulated deficit of $46.2 million, primarily as a result of research and development and general and administrative expenses. We expect to incur substantial losses from operations in the foreseeable future as we continue our research and development efforts, advance AVA-101 and other product candidates through preclinical and clinical development, manufacture clinical study materials, seek regulatory approval and prepare for, and if approved, proceed to commercialization. We are at an early stage of development and may never be successful in developing or commercializing our product candidates.

While we may in the future generate revenue from a variety of sources, including license fees, milestone and research and development payments in connection with strategic partnerships, and potentially revenue from approved product sales, we have not yet generated any revenue from approved therapeutic product candidates.

We have no manufacturing facilities, and all of our manufacturing activities are contracted out to a third party. Additionally, we currently utilize third-party clinical research organizations (CROs) to carry out our clinical development and we do not yet have a sales organization.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of AVA-101 and any additional product candidates. Specifically, we have incurred and we expect to continue to incur substantial expenses in connection with our existing Phase 2a clinical trial and any Phase 2b and Phase 3 clinical trials that we may conduct for AVA-101. We will need substantial additional funding to support our operating activities as we advance AVA-101 and other potential product candidates through clinical development, seek regulatory approval and prepare for and, if approved, proceed to commercialization. Adequate funding may not be available to us on acceptable terms, or at all.

On January 13, 2015, we completed a Follow-on Offering and we received net proceeds of approximately $130.6 million, after underwriting discounts, commissions and offering expenses. As of March 31, 2015, we had $201.8 million in cash and cash equivalents and $88.3 million of marketable securities. We believe that we have sufficient funds to continue operations through at least the next twelve months.

Revenue

To date we have not generated any revenue from the sale of our products. In May 2014, we entered into a multi-year license and development agreement with Regeneron. Under the terms of the agreement, we received initial payments of $8.0 million that included payment for research license fees, prepaid collaboration research costs and the right of first negotiation for a potential license to develop and commercialize AVA-101. As the agreement provides for multiple deliverables, we account for this agreement as a multiple elements revenue arrangement. If deliverables do not appear to have a standalone fair value, they were combined with other deliverables into a unit of accounting with standalone fair value. We allocated the $8.0 million received to the fair values of the two units of accounting identified in the arrangement. We expect to recognize $6.5 million for research licenses and related research and development services ratably over the associated period of performance, which is the maximum research period of eight years. As there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, we will recognize revenue on a straight-line basis over the eight-year performance period. The remaining $1.5 million allocated to the second unit of accounting for the time-limited right of first negotiation for AVA-101 is deferred and will be recognized during the period when Regeneron has exclusive access to the results of Phase 2a clinical trials.

During the three months ended March 31, 2015, the Company recognized $0.2 million under the Regeneron agreement. Prior to that period, we had previously only recognized revenue in connection with a license agreement for our technology and under government grants.

Our ability to generate product revenue and become profitable depends upon our ability to successfully develop and commercialize our product candidates. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the amount or timing of product revenue. Even if we are able to generate revenue from the sale of our products, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Research and Development Expenses

Conducting a significant amount of research and development is central to our business model. Research and development expenses include certain payroll and personnel expenses, stock-based compensation expense, laboratory supplies, consulting costs, external contract research and development expenses, including expenses incurred under agreements with CROs, the cost of acquiring, developing and manufacturing clinical study materials and overhead expenses, including rent, equipment depreciation, insurance and utilities.

Research and development costs are expensed as incurred. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

We estimate preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. We estimate the amounts incurred through communications with third party service providers and our estimates of accrued expenses as of each balance sheet date are based on information available at the time. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly.

As we pursue the clinical development of our lead product candidate, AVA-101, the amount of research and development expenses will continue to grow. Product candidates in later stages of clinical development have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late-stage clinical trials. Accordingly, we plan to increase our research and development expenses for the foreseeable future as we seek to complete the development and commercialization of AVA-101. The successful development and commercialization of AVA-101 is highly uncertain and we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of AVA-101 at this time. Clinical development timelines, the probability of success and development and commercialization costs can differ materially from expectations.

We received refundable tax credits from the Australian tax authorities in connection with certain research costs incurred by our subsidiary conducting research in Australia. These refunds do not depend on our taxable income or tax position and therefore we do not account for them under an income tax accounting model. We recognize such refunds in the period when qualified expenses are incurred as a reduction of research expenses. We have recorded the reimbursement from the Australian tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss for the applicable period.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, stock-based compensation, professional fees for legal, consulting, audit and tax services, rent and other general operating expenses not otherwise included in research and development expenses. We anticipate general and administrative expenses will increase in future periods as we invest in the infrastructure needed to support continued research and development activities and potential commercialization of our product candidates. We also anticipate increased expenses related to audit, legal and regulatory functions, as well as director and officer insurance premiums and investor relations costs associated with being a public reporting company.

Other Income (Expense), Net

Other income (expense), net is comprised mainly of changes in the fair value of common stock warrant liabilities and preferred stock warrant liabilities in 2014 and interest income in 2015. At the time of the IPO, all outstanding warrants were exercised, and as a consequence, the Company does not expect to have any other income (expense), net related to changes in the fair value of warrant liabilities in future periods.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations are based upon our unaudited condensed consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP). The preparation of these condensed consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. On an on-going basis, we evaluate our critical accounting policies and estimates. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable in 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 and conditions. Our significant accounting policies are more fully described in Note 2 of the accompanying unaudited condensed consolidated financial statements and in Note 2 to our audited consolidated financial statements contained in our Annual Report on Form 10-K (Annual Report) as filed with the SEC, on March 5, 2015.

During the three months ended March 31, 2015, we began to invest in marketable securities, and as a result, have adopted new marketable securities accounting policy as discussed in Note 2 of the accompanying unaudited condensed consolidated financial statements. There have been no other changes in our critical accounting policies since the end of fiscal year 2014.

Results of Operations

Comparison of the Three Month Periods Ended March 31, 2015 and 2014 (in thousands)

	Three Months Ended March 31,		Change
	2015	2014	
Collaboration and license revenue	$ 203	$ 30	$ 173
Operating expenses:			
Research and development	5,621	910	4,711
General and administrative	4,143	726	3,417
Total operating expenses	9,764	1,636	8,128
Operating loss	(9,561)	(1,606)	(7,955)
Interest expense	—	(14)	14
Other income (expense), net	52	(6)	58
Change in fair value of warrant liabilities	—	(37)	37
Total other income (expense), net	52	(57)	109
Net loss	$(9,509)	$(1,663)	$(7,846)

Revenue

Collaboration and license revenue for the three months ended March 31, 2015 increased by $0.2 million over the prior year period, as we recognized revenue from the Regeneron agreement. This revenue was related to the current quarter research services, which is being recognized ratably over our performance period. Collaboration and license revenue for the three months ended March 31, 2014 was related to a $30,000 license fee from licensing of certain of our intellectual property under a licensing agreement entered into during the first quarter of 2014.

Research and Development Expense

Research and development expense increased to $5.6 million for the three months ended March 31, 2015 from $0.9 million for the three months ended March 31, 2014, primarily due to expense increases of $0.2 million in stock-based compensation, $1.8 million in salaries and related expenses due to increased employee headcount, $1.7 million in drug product process development expenses and laboratory expenses and $1.0 million in external consulting expenses and research studies, as we expanded our research organization.

For the periods presented, substantially all of our research and development expense related to development activities for AVA-101, for the treatment of wet AMD, and our other potential product candidates in our development program. We expect research and development expenses to increase in future periods as we continue to invest in our pipeline products and AVA-101 late-stage clinical trials.

General and Administrative Expense

General and administrative expense increased to $4.1 million for the three months ended March 31, 2015 from $0.7 million for the three months ended March 31, 2014. The increase in general and administrative expense was primarily due to expense increases of $1.1 million in salaries and related expenses related to increased employee headcount, $0.4 million in stock-based compensation expenses, $1.2 million in public company-related expenses and overhead and $0.5 million in consulting and professional service expenses, as we expanded our operations.

We expect general and administrative costs to increase in future periods, reflecting both the increased costs in connection with the future commercialization of AVA-101 and our pipeline products, as well as an expanded infrastructure and increased professional fees associated with being a public company.

Liquidity and Capital Resources and Plan of Operations

We have not generated positive cash flow or net income from operations since our inception and, at March 31, 2015, we had an accumulated deficit of $46.2 million, primarily as a result of research and development and general and administration expenses. On January 13, 2015, we completed a Follow-on Offering and we received net proceeds of approximately $130.6 million, after underwriting discounts, commissions and offering expenses. As of March 31, 2015, we had $201.8 million in cash and cash equivalents and $88.3 million of marketable securities invested in a money market fund, certificates of deposit, U.S. Treasury and U.S. government agencies securities with maturities of 12 months or less. We believe that our existing cash and cash equivalents and marketable securities as of March 31, 2015 will be sufficient to fund our operations through at least the next twelve months.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates and ongoing internal research and development programs. In order to complete our planned preclinical and clinical trials and complete the process of obtaining regulatory approval for our lead product candidate, as well as to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital in the future could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials for AVA-101 and our other product candidates in development;
- the outcome, timing of and costs involved in, seeking and obtaining approvals from the Food and Drug Administration (FDA) and other regulatory authorities, including the potential for the FDA and other regulatory authorities to require that we perform more studies than those that we currently expect;
- the ability of our product candidates to progress through clinical development activities successfully;
- our need to expand our research and development activities;
- the rate of progress and cost of our commercialization of our products;
- the cost of preparing to manufacture our products on a larger scale;
- the costs of commercialization activities including product sales, marketing, manufacturing and distribution;
- the degree and rate of market acceptance of any products launched by us or future partners;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need to implement additional infrastructure and internal systems;
- our ability to hire additional personnel;
- our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
- the emergence of competing technologies or other adverse market developments.

If we are unable to raise additional funds when needed, we may be required to delay, reduce or terminate some or all of our development programs and clinical trials. We may also be required to sell or license other technologies or clinical product candidates or programs that we would prefer to develop and commercialize ourselves.

Cash Flows

	Three Month Periods Ended March 31,	
	2015	2014
	(in thousands)	
Cash Flows from Continuing Operations:		
Net cash used in operating activities	$ (7,742)	$ (1,347)
Net cash used in investing activities	(88,781)	(47)
Net cash provided by financing activities	138,975	1,000
Net increase (decrease) in cash and cash equivalents	$ 42,445	$ (395)

During the three months ended March 31, 2015, net cash used in operating activities was $7.7 million, primarily as a result of the net loss of $9.5 million offset by $0.8 million in non-cash charge related to stock-based compensation and by $1.0 million in net increase in accounts payable and accrued expenses. During the three months ended March 31, 2014, net cash used in operating activities was $1.3 million, primarily as a result of the net loss of $1.7 million during the period offset by $0.4 million in net increase in accounts payable and accrued expenses.

Net cash used in investing activities for the three months ended March 31, 2015 primarily relates to the purchases of marketable securities of $88.4 million. Purchases of property and equipment were $0.4 million and $47,000 during the three months ended March 31, 2015 and 2014, respectively. The purchases of property and equipment consisted primarily of acquisition of laboratory equipment to support our research and development activities.

The net cash provided by financing activities during the three month period ended March 31, 2015 of $139.0 million was primarily related to $130.6 million net proceeds from our Follow-on Offering and $8.3 million from sale of common shares. Net cash provided by financing activities for the three months ended March 31, 2014 of $1.0 million was related to proceeds from the issuance of our related-party convertible notes.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

There have not been any material changes to our exposure to market risk during the three-month period ended March 31, 2015. For additional information regarding market risk, refer to the *Qualitative and Quantitative Disclosures About Market Risk* section of our Annual Report on Form 10-K.

Item 4. Controls and Procedures

Evaluation of disclosure controls and procedures. Management, including our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of March 31, 2015. The evaluation of our disclosure controls and procedures included a review of our processes and implementation and the effect on the information generated for use in this Quarterly Report on Form 10-Q. In the course of this evaluation, we sought to identify any material weaknesses in our disclosure controls and procedures to determine whether we had identified any acts of fraud involving personnel who have a significant role in our disclosure controls and procedures, and to confirm that necessary corrective action, including process improvements, was taken. This type of evaluation is done quarterly so that our conclusions concerning the effectiveness of these controls can be reported in our periodic reports filed with the SEC. The overall goals of these evaluation activities are to monitor our disclosure controls and procedures and to make modifications as necessary. We intend to maintain these disclosure controls and procedures, modifying them as circumstances warrant.

Based on that evaluation, the Chief Executive Officer and Chief Financial Officer concluded that as of March 31, 2015, the Company's disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is (i) recorded, processed, summarized and reported as and when required and (ii) accumulated and communicated to our management, including the Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely discussion regarding required disclosure.

Changes in internal control over financial reporting. There have been no significant changes in our internal control over financial reporting during the three months ended March 31, 2015 that have materially affected or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Controls and Procedures

Our management, including the Chief Executive Officer and the Chief Financial Officer, does not expect that our disclosure controls and procedures and our internal controls will prevent all error and all fraud. A control system, no matter how well designed and operated, can only provide reasonable assurances that the objectives of the control system are met. The design of a control system reflects resource constraints; the benefits of controls must be considered relative to their costs. Because there are inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been or will be detected. As these inherent limitations are known features of the financial reporting process, it is possible to design into the process safeguards to reduce, though not eliminate, these risks. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns occur because of simple error or mistake. Controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls is based in part upon certain assumptions about the likelihood of future events. While our disclosure controls and procedures are designed to provide reasonable assurance of achieving their objectives, there can be no assurance that any design will succeed in achieving its stated goals under all future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with the policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

We intend to review and evaluate the design and effectiveness of our disclosure controls and procedures on an ongoing basis and to improve our controls and procedures over time and to correct any deficiencies that we may discover in the future. While our Chief Executive Officer and Chief Financial Officer have concluded that, as of March 31, 2015, the design of our disclosure controls and procedures, as defined in Rule 13a-15(e) under the Exchange Act, was effective, future events affecting our business may cause us to significantly modify our disclosure controls and procedures.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently a party to any material litigation or other material legal proceedings.

Item 1A. Risk Factors

Risks Related to Our Financial Position and Need for Capital

We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since we were founded in 2006 and expect to incur significant losses for the foreseeable future as we continue our clinical trial and development programs for AVA-101, a gene therapy product targeting vascular endothelial growth factor (VEGF) currently under development for the treatment of wet age-related macular degeneration (AMD), and our other product candidates. Our net loss for 2014 was $25.4 million and for the three months ended March 31, 2015 was $9.5 million. As of March 31, 2015, we had an accumulated deficit of $46.2 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities and, if AVA-101 or any of our other product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize AVA-101 or other future product candidates. We do not currently have the required approvals to market AVA-101 or any other future product candidates, and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize AVA-101 and our other product candidates.

We will require substantial future capital in order to complete the remaining clinical development for AVA-101 and our other product candidates and to potentially commercialize these product candidates. We expect our spending levels to increase in connection with our clinical trials of AVA-101, as well as other corporate activities. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the type, number, scope, progress, expansion costs, results of and timing of our planned clinical trials of AVA-101 or any of our other product candidates which we are pursuing or may choose to pursue in the future;
- the need for, and the progress, costs and results of, any additional clinical trials of AVA-101 and our other product candidates we may initiate based on the results of our planned clinical trials or discussions with the FDA, including any additional trials the FDA or other regulatory agencies may require evaluating the safety of AVA-101 and our other product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining or maintaining manufacturing for AVA-101 and our other product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales and marketing capabilities and enhanced internal controls over financial reporting;
- the terms and timing of establishing collaborations, license agreements and other partnerships;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- the effect of competing technological and market developments;
- our ability to establish and maintain partnering arrangements for development; and
- the costs associated with being a public company.

Some of these factors are outside of our control. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of our clinical trials and remaining development program through commercial introduction. We expect that we will need to raise additional funds in the future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through collaboration agreements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we will be unable to complete the planned clinical trials for AVA-101 and our other product candidates and we may be required to significantly curtail some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or some of our technologies or otherwise agree to terms unfavorable to us.

Risks Related to the Discovery and Development of Our Product Candidates

Our business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed.

Our product candidates are in the early stage of development and will require additional preclinical studies, substantial clinical development and testing, manufacturing bridging studies and process validation and regulatory approval prior to commercialization. We have only one product candidate that has been the focus of advanced development efforts: AVA-101, a recombinant adeno-associated vector type 2 (AAV2) encoding the anti-VEGF protein sFLT-1. Successful continued development and ultimate regulatory approval of AVA-101 is critical for our future business success. We have invested, and will continue to invest, a significant portion of our time and financial resources in the development of AVA-101. We will need to raise sufficient funds for, and successfully enroll and complete, our planned clinical trials of AVA-101 in wet AMD subjects. The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for AVA-101;
- we may not be able to provide evidence of efficacy and safety for AVA-101;
- we do not know the degree to which AVA-101 will be accepted as a therapy for wet AMD, even if approved;

- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;
- subjects in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to AVA-101;
- if approved for treatment of wet AMD, AVA-101 will likely compete with other treatments then available, including the off-label use of products already approved for marketing and other therapies currently available or which may be developed; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Of the large number of biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a Biologics Licensing Application (BLA) or a New Drug Application (NDA) to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market AVA-101, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that AVA-101 will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, AVA-101, we may not be able to generate sufficient revenue to continue our business.

We are conducting, and may in the future conduct, clinical trials for AVA-101 and other product candidates in sites outside the United States and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. For example, we are currently conducting a Phase 1/2a trial for AVA-101 with LEI in Australia.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The study population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical studies conducted outside of the United States must be representative of the population for whom we intend to label the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the studies also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials for AVA-101 or any other product candidates, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of AVA-101 or any other product candidates. The FDA may also determine that additional safety or other data are needed before we may commence a Phase 2b clinical trial which could require us to conduct additional trials before we proceed.

Our Ocular BioFactory is based on a novel gene therapy technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only one gene therapy product has been approved in Europe.

We have concentrated our research and development efforts on our Ocular BioFactory, which is a gene therapy platform, and our future success depends on the successful development of product candidates based on this platform. There can be no assurance that any development problems we experience in the future related to our Ocular BioFactory platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical study requirements of the FDA, the European Medicines Agency (EMA) and other regulatory agencies and the criteria these regulators may use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. As of the date of this Quarterly Report on Form 10-Q, the FDA has not approved any gene therapy products for sale and only one gene therapy product has been approved in the Western world, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either Europe or the United States. Approvals by the EMA may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products may change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research (CBER) to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical studies conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health (NIH) may also be subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee (RAC). Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation.

Conversely, the FDA can put an Investigational New Drug application (IND) on clinical hold even if the RAC has provided a favorable review. Also, before a clinical study can begin at an NIH-funded institution, that institution's institutional review board (IRB) and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we may be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

All of our product candidates are still in preclinical or early-stage clinical development. If we are unable to commercialize our product candidates or if we experience significant delays in obtaining regulatory approval for, or commercializing, any or all of our product candidates, our business will be materially and adversely affected.

All of our product candidates are still in preclinical and early-stage clinical development. Our ability to generate product revenue will depend heavily on our ability to successfully develop and commercialize these product candidates. We do not expect that such commercialization of any of our product candidates will occur for at least the next several years, if ever. Our ability to commercialize our product candidates effectively will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our product candidates;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States;
- establishing commercial manufacturing capabilities, for example, by making arrangements with third-party manufacturers;
- successfully launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payers;
- establishing market share while competing with other therapies;
- a continued acceptable safety profile of our products following regulatory approval;
- maintaining compliance with post-approval regulation and other requirements; and
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates.

If we, or our collaborators, do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to commercialize our product candidates, which would materially and adversely affect our business, financial condition and results of operations.

We may not be successful in our efforts to identify or discover additional product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our Ocular BioFactory platform. Although our AVA-101 product candidate is currently in clinical development, our research programs, including those subject to our collaboration with Regeneron, may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

We have not tested any of our internally-developed viral vectors, or product candidates derived from these viral vectors, in clinical trials.

Drug development has inherent risk. Our lead product AVA-101 produced in mammalian-cell based manufacturing system is currently being evaluated in a Phase 1/2a human clinical trial. However, neither AVA-101 manufactured in the baculovirus expression system (BVES) system nor our other product candidates have ever been evaluated in human clinical studies, and we may experience unexpected results in the future. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates containing our proprietary vectors are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including AVA-101, may not have favorable results in later clinical trials, if any, or receive regulatory approval.

If our proprietary vectors are not shown to be safe and effective in targeting retinal tissue, we may not realize the value of our investment in directed evolution technology. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

We cannot be certain that any of our planned clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

AVA-101 and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials;
- we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;
- we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates.

If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. We will be required to identify and enroll a sufficient number of subjects with wet AMD for each of our planned clinical trials of AVA-101. Potential subjects for AVA-101 may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies. We also may encounter difficulties in identifying and enrolling wet AMD subjects with a stage of disease appropriate for our planned clinical trials. In addition, we and our collaboration partner, Regeneron, are developing AVA-311 for the treatment of X-linked retinoschisis (XLRS), an orphan indication. Enrollment of eligible subjects with orphan diseases may be limited or slower than we anticipate in light of the small subject populations involved. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or other foreign regulatory agencies. In addition, the process of finding and diagnosing subjects may prove costly.

We expect to initiate a Phase 2b clinical trial for AVA-101 in the United States in the second half of 2015. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical trials for similar patient populations or available approved therapies, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed.

Trials using early versions of retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events. For example, generalized public backlash developed against gene therapy following the death in September 1999 of an 18-year-old who had volunteered for a gene therapy experiment at the University of Pennsylvania. Researchers at the university had infused the volunteer's liver with a gene aimed at reversing a rare metabolic disease of the liver. The procedure triggered an extreme immune-system reaction that caused multiple-organ failure in a very short time, leading to the first death to occur as a direct result of a gene therapy experiment. In addition, in 2003, 20 subjects treated for X-linked severe combined immunodeficiency in two gene therapy studies using a murine gamma-retroviral vector showed correction of the disease, but the studies were terminated after five subjects developed leukemia (four of whom were subsequently cured). The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer (often leukemia). Using molecular diagnostic techniques, it was determined that clones from these subjects showed retrovirus insertion in proximity to the promoter of the LMO2 proto-oncogene. Earlier generation retroviruses like the one used in these two studies have been shown to preferentially integrate in regulatory regions of genes that control cell growth. Our inability to enroll a sufficient number of subjects for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

We believe we have appropriately accounted for the above factors in our trials when determining expected clinical trial timelines, but we cannot assure you that our assumptions are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

The occurrence of serious complications or side effects in connection with use of our product candidates, either in clinical trials or post-approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business, prospects, operating results and financial condition.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Various illnesses, injuries, and discomforts have been reported from time-to-time during clinical trials of our product candidates. It is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, operating results and financial condition.

AVA-101 is being studied in diseases of the eye in addition to AMD. There are many potential safety concerns associated with significant blockade of VEGF that may limit our ability to successfully develop and/or commercialize AVA-101. These serious and potentially life-threatening risks, based on clinical and preclinical experience of VEGF inhibitors, include bleeding, intestinal perforation, hypertension, proteinuria, congestive heart failure, heart attack, stroke and geographic atrophy. In addition, patients given infusions of any protein may develop severe hypersensitivity reactions or infusion reactions. Other VEGF inhibitors have reported side effects that became evident only after large-scale trials or after marketing approval when large numbers of patients were treated. There are risks in treating patients with gene therapy vectors, including adeno-associated virus (AAV), such as inflammation, cytotoxic T-cell response, anti-AAV antibodies and immune response to the expressed transgene, including T-cell responses and/or auto-antibodies against sFLT-1. There are risks inherent in the subretinal administration of drugs like AVA-101, which can cause injury to the eye and other complications. For example, in our Phase 1/2a trials of AVA-101 in wet AMD, the most frequent ocular adverse events to date have been subconjunctival hemorrhage, vitreous hemorrhage, cataract progression and intra-ocular inflammation.

There are also risks inherent in subretinal injections, including subretinal injections with AVA-101, such as intraocular inflammation, cataract, sterile and culture positive endophthalmitis, retinal detachment, retinal tear and other side effects. Serious complications or serious, unexpected side effects in connection with the use of AVA-101 could materially harm our business, prospects' operating results and financial condition.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We are dependent on third parties to conduct the Phase 2 and Phase 3 clinical trials for AVA-101 and preclinical and clinical trials for our other future product candidates, and, therefore, the timing of the initiation and completion of these trials is controlled by such third parties and may occur at times substantially different from our estimates. Specifically, we use clinical research organizations (CROs) to conduct our clinical trials and rely on medical institutions, clinical investigators, CROs and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data.

There is no guarantee that any CROs, investigators or other third parties on which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, fails to meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit by the FDA. Any such delay or rejection could prevent us from commercializing AVA-101 or our other future product candidates.

We expect to rely on third parties to conduct some or all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies required to support future IND submissions and approval of our product candidates.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products.

We and our contract manufacturer are subject to significant regulation with respect to manufacturing our products. The manufacturing facility on which we rely may not continue to meet regulatory requirements and may have limited capacity.

We currently have relationships with a single supplier for the manufacturing of our viral vectors and product candidates. The supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities. All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturer for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with current Good Manufacturing Practice (cGMP). These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturer must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current Good Laboratory Practice regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Our contract manufacturer has not produced a commercially-approved product and therefore has not obtained the requisite FDA approvals to do so. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect our manufacturing facilities or those of our third-party contractors involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If the facility does not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Such violations could also result in civil and/or criminal penalties. Any such remedial measures or other civil and/or criminal penalties imposed upon us or third parties with whom we contract could materially harm our business.

If we or our third-party manufacturer fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, revocation of a pre-existing approval, other civil or criminal penalties or closing one or more manufacturing facilities. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks Related to Commercialization of Our Product Candidates

Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials in the United States for our product candidates, we need to submit the results of preclinical testing to the FDA, along with other information including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND. We may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our plans for our clinical trials. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND, which may lead to additional delays and increase the costs of our preclinical development. Delays in the commencement or completion of our planned clinical trials for AVA-101 or other product candidates could significantly affect our product development costs. We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA failing to grant permission to proceed or placing the clinical trial on hold;

- subjects failing to enroll or remain in our trial at the rate we expect;
- subjects choosing an alternative treatment for the indication for which we are developing AVA-101 or other product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- a facility manufacturing AVA-101, any of our other product candidates or any of their components being ordered by the FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of cGMP or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practice or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;
- inspections of clinical trial sites by the FDA or the finding of regulatory violations by the FDA or an IRB that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire trial or that prohibit us from using some or all of the data in support of our marketing applications;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of AVA-101 or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of our clinical trials, or if we, the FDA or other regulatory authorities, the IRB, other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for a product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. For example, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of AVA-101 or other product candidates could be significantly reduced.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones will be based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline.

Final marketing approval for AVA-101 or our other product candidates by the FDA or other regulatory authorities for commercial use may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenue.

After the completion of our clinical trials and, assuming the results of the trials are successful, the submission of a BLA, we cannot predict whether or when we will obtain regulatory approval to commercialize AVA-101 or our other product candidates, and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize AVA-101 or our other product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for AVA-101 or our other product candidates. In addition, we may experience delays or rejections based upon additional government regulation

from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. If marketing approval for AVA-101 or our other product candidates is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

Even if we obtain marketing approval for AVA-101 or any other product candidate, they could be subject to restrictions or withdrawal from the market, and we may be subject to 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.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. Following approval, if at all, of AVA-101 or any other product candidates, such candidate will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for AVA-101 or any other product candidate that may receive regulatory approval, if any, fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product or request us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue. The FDA has the authority to require a risk evaluation and mitigation strategy plan as part of a BLA or NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry.

In addition, if AVA-101 or any of our other product candidates is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Even if we receive regulatory approval we still may not be able to successfully commercialize AVA-101 or any other product candidate, and the revenue that we generate from its sales, if any, could be limited.

Even if AVA-101 or any of our other product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payers or the medical community. Coverage and reimbursement of our product candidates by third-party payers, including government payers, is also generally necessary for commercial success. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;

- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new formulation by health care providers and their patients;
- the prevalence and severity of any adverse effects;
- new procedures or methods of treatment that may be more effective in treating or may reduce the incidences of wet AMD or other conditions for which our products are intended to treat;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain and maintain sufficient third-party coverage and reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payers;
- unfavorable publicity relating to the product candidate; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage and reimbursement.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payers or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payers on the benefits of AVA-101 or any of our other product candidates may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidate will depend on our ability to manufacture our products, differentiate our products from competing products and defend and enforce our intellectual property rights relating to our products.

If the market for AVA-101 for the treatment of wet AMD is smaller than we believe it is, our future revenue may be adversely affected, and our business may suffer.

If the size of the market for wet AMD is smaller than we anticipate, we may not be able to achieve profitability and growth. While we are initially targeting AVA-101 for the treatment of wet AMD, a disease we believe to be the most common cause of vision loss in adults over the age of 50 in developed countries, our projections of the number of people who have wet AMD, as well as the subset of people with these diseases who have the potential to benefit from treatment with wet AMD, are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations and market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

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

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payers for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payer may depend upon a number of factors including the third-party payer's determination that use of a product candidate is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product candidate from a government or other third-party payer is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of the applicable product candidate to the payer. We may not be able to provide data sufficient to gain acceptance with respect to

coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, reimbursement amounts may reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payers are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. By way of example, the Medicare Prescription Drug Improvement and Modernization Act of 2003 (MMA) changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs, including drugs currently on the market used by physicians to treat wet AMD and likely AVA-101, if approved. As a result of this legislation and the expansion of federal coverage of drug products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payers. These cost reduction initiatives and other provisions of the MMA could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively referred to as the Affordable Care Act, was enacted with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care organizations and established annual fees and taxes on manufacturers of certain prescription drugs.

Other legislative changes have also been proposed and adopted in the U.S. since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken.

We expect that additional healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our products, if approved, or additional pricing pressures.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of health care may adversely affect:

- the demand for any product candidates for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our product candidates;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

Our product candidates are designed to provide therapeutic benefit after a single administration and, therefore, the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

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

Although the development and commercialization of AVA-101 for the treatment of wet AMD is our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to ocular diseases. We will evaluate internal opportunities from our compound libraries, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from ocular diseases such as diabetic macular edema (DME), retinal vein occlusion (RVO), glaucoma, XLRS or other disorders with high unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

We are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

The process of manufacturing our products is complex, highly regulated and subject to several risks, including:

- The manufacturing of biologics is extremely susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment or vendor or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing facility in which our products are made, such manufacturing facility may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facility in which our products are made could be adversely affected by equipment failures, labor shortages, contaminants, raw materials shortages, natural disasters, power failures and numerous other factors.
- We and our contract manufacturer must comply with the FDA's cGMP regulations and guidelines. We and our contract manufacturer may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our contract manufacturer are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or any delay, interruption or other issues that arise in the manufacture, fill-finish, packaging or storage of our products as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products. This may lead to significant delays in the availability of products for our clinical studies or the termination or hold on a clinical study, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could be costly and damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our products and/or may be subject to product recalls, seizures, injunctions or criminal prosecution.
- Our product candidates are biologics and require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be adequately characterized prior to manufacturing the final product. As a result, an assay of the finished product is not sufficient to ensure that the product will perform in the intended manner. Accordingly, we expect to employ multiple steps to attempt to control our manufacturing process to assure that the process works and the product or product candidate is made strictly and consistently in compliance with the process.
- Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory.
- Some of the raw materials required in our manufacturing process are derived from biological sources. Such raw materials are difficult to procure and may also be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt commercialization.
- Any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. We may encounter problems achieving adequate or clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

We may not be successful in establishing and maintaining development or other strategic collaborations, which could adversely affect our ability to develop and commercialize product candidates.

We have entered into development or other strategic collaborations with major biotechnology or pharmaceutical companies. For example, our research collaboration and license agreement with Regeneron, which was announced in May 2014, covers up to eight distinct therapeutic targets, in which we could earn up to $80.0 million in development and regulatory milestones for product candidates directed toward each therapeutic target, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

Some of our strategic partners may terminate any agreements they enter into with us, and we may not be able to adequately protect our rights under these agreements. Furthermore, our strategic partners have negotiated for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do.

Moreover, if we fail to maintain development or other strategic collaborations related to our product candidates that we may choose to enter into:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly, and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development of any such product candidates.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of our product candidates. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, 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 AVA-101 or our other product candidates because third parties may view the risk of failure in future clinical trials as too significant or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such development partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are disappointing. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market.

If our competitors develop treatments for the target indications of our product candidates that are approved more quickly than ours, marketed more successfully or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

We operate in highly competitive segments of the biopharmaceutical markets. We face competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies as well as with new treatments that may be introduced by our competitors. There are a variety of drug candidates in development for the indications that we intend to test. Many of our competitors have significantly greater financial, product candidate development, manufacturing and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. In addition, universities and private and public research institutes may be active in wet AMD research, and some could be in direct competition with us. We also may compete with these organizations to recruit management, scientists and clinical development personnel. We will also face competition from these third parties in establishing clinical trial sites, registering subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

New developments, including the development of other pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. Competition in drug development is intense. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available.

Even if we obtain regulatory approval for our product candidates, the availability and price of our competitors' products could limit the demand, and the price we are able to charge, for our product candidates. For example, EYLEA is currently available in the United States for treatment of wet AMD and macular edema following central retinal vein occlusion (CRVO), and in the United Kingdom, Germany, Switzerland, Australia, Japan and certain other countries for the treatment of wet AMD. Additionally, marketing approval has been obtained in the EU for EYLEA for the treatment of visual impairment due to macular edema secondary to CRVO. We will not achieve our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances. Our inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, prospects, financial condition and results of operations.

Our potential competitors in these diseases may be developing novel immune modulating therapies that may be safer or more effective than AVA-101 or our other product candidates. For example, AVA-101 will compete with a variety of therapies currently marketed and in development for wet AMD, using therapeutic modalities such as biologics, small molecules and gene therapy. Lucentis, EYLEA and Avastin® are anti-VEGF therapies that are well established and widely accepted by physicians, patients and third-party payers as the standard of care for the treatment of wet AMD. There are several other companies with marketed products or products in development for the treatment of wet AMD, including Allergan, Iconic Therapeutics, Inc., LPath Therapeutics Inc., Novartis AG, Ocular Therapeutix, Inc., Ophthotech Corporation, Hoffmann-La Roche Ltd., Neurotech Pharmaceuticals, Inc., Regeneron, Santen Pharmaceuticals Co., Ltd., Valeant Pharmaceuticals North America LLC, ReGenX Biosciences LLC, Ohr Pharmaceuticals, Inc. and Mesoblast Limited.

Our preclinical product candidates are being developed for the treatment of prevalent or rare ophthalmic diseases, such as the prevention of wet AMD and XLRS, for which there are no approved therapies. However, there are multiple companies developing gene therapies for ophthalmic diseases, including Applied Genetic Technologies Coporation, Asklepios BioPharmaceutical Inc., Eos Neuroscience, Inc., GenSight Biologics, Genzyme Corporation, Hemera Biosciences, Inc., RetroSense Therapeutics, LLC, Spark Therapeutics, Inc., Oxford Biomedica plc, Sanofi-Aventis S.A., NightStaRx Limited and 4D Molecular Therapeutics, LLC.

We have no sales, marketing or distribution capabilities, and we may have to invest significant resources to develop these capabilities.

We have no internal sales, marketing or distribution capabilities. If AVA-101 or any of our other product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We may have to invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that AVA-101 or any of our other product candidates will be approved, if at all. We may not be able to hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms or at all. Even if we determine to perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by AVA-101 or any other product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product candidates. In some foreign countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Risks Related to Our Business Operations

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of AVA-101 and our product candidates or adversely affect our ability to conduct our business or obtain further marketing approvals for AVA-101 and marketing approvals for our product candidates.

Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing symptomatic treatments they are already familiar with and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. Although none of our current product candidates utilize the gamma-retroviruses used in the 2003 studies, our product candidates do use a viral vector delivery system. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

Adverse events in our clinical trials or those conducted by other parties, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any such adverse events occur, commercialization of AVA-101 or further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

We are dependent on the services of our President and Chief Executive Officer, Thomas W. Chalberg, Jr., Ph.D., and other key executives, and if we are not able to retain these members of our management or recruit additional management, clinical and scientific personnel, our business will suffer.

We are dependent on the principal members of our management and scientific staff. The loss of service of any of our management could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management, particularly our President and Chief Executive Officer, Dr. Chalberg, and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including Dr. Chalberg, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our clinical development and commercialization efforts. Our success also depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations.

Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

If we fail to effectively integrate our new executive officers into our organization, the future development and commercialization of our product candidates may suffer, harming future regulatory approvals, sales of our product candidates or our results of operations.

Our current management team has only been working together for a relatively short period of time and some of our current management team have been employed by us for less than a year. Moreover, we expect to continue to expand our management team in the future. Our future performance will depend, in part, on our ability to successfully integrate recently and subsequently hired executive officers into our management team and their ability to develop and maintain an effective working relationship. Our failure to integrate these individuals with other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. In addition to the competition for personnel, the San Francisco Bay Area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

We may encounter difficulties in managing our growth and expanding our operations successfully.

Because we have only 64 full-time employees as of April 30, 2015, we will need to grow our organization substantially to continue development and pursue the potential commercialization of AVA-101 and our other product candidates, as well as function as a public company. As we seek to advance AVA-101 and other product candidates, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain additional internal capabilities. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, clinical and regulatory, financial, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to so accomplish could prevent us from successfully growing our company.

If we fail to comply with applicable state and federal healthcare laws, we may be subject to civil or criminal penalties and/or exclusion from federal healthcare programs.

In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include anti-kickback, false claims, physician payment transparency and privacy and security laws and regulations. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced price items and services. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formula managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Many states have similar laws that apply to their state health care programs as well as private payers.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. The Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statute governing healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Additionally, the False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. The period between August 1, 2013 and December 31, 2013 was the first reporting period, and manufacturers were required to report aggregate payment data by March 31, 2014, and to report detailed payment data and submit legal attestation to the accuracy of such data by June 30, 2014. Thereafter, manufacturers must submit reports by the 90th day of each subsequent calendar year. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

In the course of conducting our business, we may also obtain certain confidential patient health information including retinal scans from subjects participating in our clinical trials. In the event of an inadvertent disclosure or security breach, we could be subject to enforcement measures, including civil and criminal penalties and fines for violations of state and federal privacy or security standards, such as HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations, including the final omnibus rule published on January 25, 2013. Additionally, certain states have adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. HIPAA, HITECH and comparable state laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. Any liability from failure to comply with the requirements of these laws, to the extent such requirements are deemed to apply to our operations, could adversely affect our financial condition. The costs of complying with privacy and security related legal and regulatory requirements are burdensome and could have a material adverse effect on our results of operations.

The need to build and maintain a robust compliance program with different compliance and/or reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

We and our development partners, third-party manufacturer and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and our development partners, third-party manufacturer and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of AVA-101 or our other product candidates.

We face an inherent risk of product liability as a result of the clinical testing of AVA-101 and our other product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if AVA-101 or our other product candidates allegedly cause injury or are 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 candidate, 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 or cease the commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for AVA-101 or our other product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a 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 AVA-101 or our other product candidates; and
- a decline in our stock price.

We currently hold $5 million in product liability insurance, which may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. 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 AVA-101 or our other product candidates. Although we plan to 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 will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may 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.

We and any of our future development partners will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we and any of our future development partners or CROs are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our future development partners report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our future development partners may fail to report adverse events we become aware of within the prescribed timeframe. We and any of our future development partners may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we and any of our future development partners fail to comply with our reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our internal computer systems, or those of our development partners, third-party clinical research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce AVA-101 and our other product candidates. Our ability to obtain clinical supplies of AVA-101 or our other product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to regulatory authorities, (2) manufacturing standards, (3) federal and state health care fraud and abuse laws and regulations or (4) laws that require the reporting of financial information or data accurately. Specifically, sales, marketing, and business arrangements in the health care 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. Activities subject to these laws also involve improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Relating to Our Intellectual Property

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies and universities.

We currently are heavily reliant upon licenses of certain patent rights and proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide adequate rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. For example, the license granted to us by the Regents to make, have made, use, offer for sale, import, export and sell products covered by certain patent rights licensed to us under our agreement with the Regents is limited to the United States. The license is also limited to the Regents' interest in the licensed patent rights which are co-owned by Chiron Corporation (Chiron). As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories not included in our licenses to patents.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, we must obtain consent from the Regents before we can enforce patent rights licensed to us by the Regents. While such consent may not be unreasonably withheld, the Regents may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

The patent rights subject to our exclusive license with the Regents are jointly owned by Chiron Corporation.

We currently have a license to the Regents' undivided interest in certain patent rights relating to the use of recombinant gene delivery vectors for treating or preventing diseases of the eye. The licensed patent rights are jointly owned by the Regents and Chiron but our license extends only the Regents' interest in such patent rights. As a result, Chiron has a right to develop and commercialize products and technology using these patent rights, and to license to third parties the right to do so. This may lead to the development and commercialization of products and technology by others that are based on technology similar to our Ocular BioFactory platform, which may impair our competitive position in the marketplace and have an adverse impact on our business.

Joint ownership of these patent rights may also limit our ability to effectively enforce our rights in these patents against alleged infringers. First, Chiron may be required to participate in any potential suit against such third party infringers but may not agree to do so. Additionally, Chiron may choose to license its interest in these patent rights to any such infringers without our consent in certain countries. Further, Chiron's joint ownership may limit the Regents' ability to prosecute related patent rights in foreign jurisdictions without the cooperation of Chiron. As a result, our business may be adversely impaired.

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and their uses as well as our ability to operate without infringing upon the proprietary rights of others. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. While we have an issued composition-of-matter patent in the United States for AVA-101, we cannot be certain that the claims in our patent applications covering composition-of-matter of our other product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged.

In addition to our composition of matter patent and applications, we have an issued method-of-use patent in the United States that encompasses AVA-101. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. However, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of AVA-101 or our other product candidates. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing AVA-101 or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this Quarterly Report on Form 10-Q, others may hold proprietary rights that could prevent AVA-101 or our other product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or

processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market AVA-101 or our other product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing AVA-101 or our other product candidates, which could harm our business, financial condition and operating results.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control the prosecution and maintenance of the patents relating to our product candidates, there may be times when the filing and prosecution activities for platform technology patents that relate to our product candidates are controlled by our licensors. For example, we do not have the right to prosecute and maintain the patent rights licensed to us under agreements with each of the Regents and Virovek Corporation, and our ability to have input into such filing and prosecution activities is limited. If these licensors or any of our future licensors fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates or companion diagnostic, our ability to develop and commercialize those product candidates and companion diagnostic may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability 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 such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. 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 research programs, license necessary technology from third parties, or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (Leahy-Smith Act), was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, inter-partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

We may fail to comply with any of our obligations under existing agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these employees and consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that our company, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of AVA-101 or other product candidates, one or more of our United States patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments). The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

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

While we have issued patents directed at AVA-101 in the United States and pending patent applications directed at AVA-101 and other product candidates in the United States and other countries, filing, prosecuting and defending patents on AVA-101 and our other product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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. For example:

- others may be able to make gene therapies 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 future collaborators 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 future collaborators 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 be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Our Common Stock

We previously identified and have remediated a material weakness in our internal control over financial reporting. If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to prepare accurate and timely consolidated financial statements being prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with the annual report for our fiscal year ending December 31, 2015. When we lose our status as an "emerging growth company" and if we reach an accelerated filer threshold, our independent registered public accounting firm will also be required to attest to the effectiveness of our internal control over financial reporting, and the related report will also be required to be included in our annual reports filed with the SEC. However, for so long as we remain an emerging growth company and also not an accelerated filer, we intend to take advantage of an exemption available to companies meeting these criteria from these auditor attestation requirements. Section 404 of the Sarbanes-Oxley Act of 2002 compliance requirements are complex and require significant documentation, testing, and possible remediation. If we (or our auditors if they are required to assess and attest to the effectiveness of our internal control over financial reporting) are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting, and the trading price of our common stock may decline.

Our management previously identified deficiencies in our internal control over financial reporting that constituted a material weakness in our internal control over financial reporting as of December 31, 2013 and which related to the design and operation of our control environment. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis. As of December 31, 2013, we did not maintain an effective control environment, which is the foundation for effective internal control over financial reporting, as evidenced by: (i) an insufficient number of personnel to perform control monitoring activities, (ii) an insufficient number of personnel with an appropriate level of knowledge of U.S. GAAP to determine that our consolidated financial statements were properly prepared in accordance with U.S. GAAP, (iii) insufficient management involvement to identify and resolve errors in recording transactions and (iv) inadequate processes for the preparation and review of our consolidated financial statements.

Subsequent to the identification of the material weakness, we hired an experienced Chief Financial Officer, Corporate Controller and additional skilled accounting and finance staff members, (b) formalized and implemented our accounting policies and internal controls and the related documentation and (c) strengthened our accounting systems, financial statements review procedures and the supervisory reviews by our management that are performed during the financial close process and which support the accurate and timely preparation of consolidated financial statements that are fairly presented in accordance with US GAAP. These improvements to our internal control infrastructure were implemented during 2014, and were in place in connection with the preparation of our consolidated financial statements for the year ended December 31, 2014.

Although we have determined that our internal control over financial reporting was effective as of December 31, 2014 we cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The NASDAQ Stock Market, the Securities and Exchange Commission (SEC) or other regulatory authorities. Failure to implement and maintain effective internal control over financial reporting, including failure to remediate any material weaknesses we or our auditors identify, could also restrict our future access to the capital markets.

An active public market for our common stock may not persist.

We completed our initial public offering (IPO) on August 5, 2014 and our follow-on offering on January 13, 2015. Prior to the IPO, there had been no public market for shares of our common stock, and an active public market for our shares may not persist. The lack of an active market may impair our stockholders' ability to sell their shares at the time they wish to sell them or at a price they consider reasonable. The lack of an active market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including those discussed in this "Risk Factors" section of this Quarterly Report on Form 10-Q and other such as:

- our ability to enroll subjects in our planned clinical trials;
- results of the clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory developments in the United States and foreign countries;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations;
- sales of our stock by insiders and stockholders;
- trading volume of our common stock;
- general economic, industry and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our clinical trial and development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting AVA-101 and our other product candidates;
- our execution of any collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- nature and terms of stock-based compensation grants; and
- derivative instruments recorded at fair value.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our failure to meet the continued listing requirements of The NASDAQ Global Market could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of The NASDAQ Global Market, such as the corporate governance requirements or the minimum closing bid price requirement, NASDAQ may take steps to de-list our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common

stock when you wish to do so. In the event of a delisting, we would expect to take actions to restore our compliance with NASDAQ's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the NASDAQ minimum bid price requirement or prevent future non-compliance with NASDAQ's listing requirements.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert control over matters subject to stockholder approval.

As of April 30, 2015, our executive officers, directors and greater than 5% stockholders, in the aggregate, own approximately 54.23% of our outstanding common stock. As a result, such persons, acting together, have the ability to control our management and affairs and substantially all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction. These persons also have the ability to control our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include:

- the authorization of the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- the limitation of the removal of directors by the stockholders;
- a staggered board of directors;
- the prohibition of stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- the elimination of the ability of stockholders to call a special meeting of stockholders;
- the ability of our board of directors to accelerate the vesting of outstanding option grants upon certain transactions that result in a change of control; and
- the establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

We do not intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

As of April 30, 2015, we have a total of 25,528,922 shares of common stock outstanding.

In addition, as of April 30, 2015, 8,454,368 shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of approximately 11.1 million shares of our outstanding common stock, or approximately 43.4% of our total outstanding common stock as of April 30, 2015, will be entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

We are an emerging growth company, and the reduced reporting requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until the last day of the fiscal year following the fifth anniversary of our IPO, although circumstances could cause us to lose that status earlier, including if we become a large accelerated filer (in which case we will cease to be an emerging company as of the date we become a large accelerated filer, which, generally, would occur if, at the end of a fiscal year, among other things, the market value of our common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter), if we have total annual gross revenue of $1.0 billion or more during any fiscal year (in which cases we would no longer be an emerging growth company as of December 31 of such fiscal year), or if we issue more than $1.0 billion in non-convertible debt during any three year period before that time (in which case we would cease to be an emerging growth company immediately). Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley and reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We have incurred and will continue to incur significant increased costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently

adopted by the SEC, and The NASDAQ Global Market to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC to adopt additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies have substantially increased our legal and financial compliance costs and make some activities more time-consuming and costly. To the extent these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

Our ability to use net operating loss carryforwards and other tax attributes may be limited by the Internal Revenue Code.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2014, the Company had U.S. federal net operating loss (NOL) carryforwards of approximately $39.6 million to offset future federal income. NOLs expire at various years beginning with 2026. As of December 31, 2014, the Company also had U.S. state NOL carryforwards of approximately $41.0 million to offset future state income. U.S. State NOLs expire at various years beginning with 2016. If over a rolling three-year period, the cumulative change in our ownership exceeds 50 percentage points (as determined under applicable Treasury regulations) under Section 382 of the Internal Revenue Code of 1986, as amended (Code), our ability to utilize our U.S. federal net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset future taxable income or taxes may be limited. We have experienced at least two ownership changes since inception and our utilization of NOL carryforwards will therefore be subject to annual limitation. Our ability to utilize our NOL carryforwards may be further limited as a result of subsequent ownership changes. Similar rules may apply under state tax laws. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

Unregistered Sales of Equity Securities

None.

Use of Proceeds

On August 5, 2014, we closed our IPO and issued 6,900,000 shares of our common stock at an initial offering price of $17.00 per share. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File Nos. 333-197133 and 333-197739), which was declared effective by the SEC on July 30, 2014. The joint book-running managers for the IPO were Jefferies LLC, Cowen and Company, LLC and Piper Jaffray & Co. The aggregate offering price to the public for the shares sold in the IPO was $117.3 million. We received net proceeds from the IPO of approximately $106.5 million, after deducting underwriting discounts and commissions of approximately $8.2 million and expenses of approximately $2.6 million payable by us. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates.

There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus filed with the SEC on July 31, 2014 pursuant to Rule 424(b) of the Securities Act. We invested the funds received in short-term, interest-bearing investment-grade securities and government securities.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

See the Exhibit Index on the page immediately preceding the exhibits for a list of exhibits filed as part of this Quarterly Report on Form 10-Q, which Exhibit Index is 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.

Date: May 13, 2015

AVALANCHE BIOTECHNOLOGIES, INC.

By: /s/ Linda C. Bain
Linda C. Bain
Chief Financial Officer
(principal financial and accounting officer)

EXHIBIT INDEX

EXHIBIT NUMBER	DESCRIPTION
3.1	Amended and Restated Certificate of Incorporation, (filed as Exhibit 3.1 to the Registrant's Current Report on Form 8-K on August 6, 2014 and incorporated herein by reference).
3.2	Amended and Restated Bylaws (filed as Exhibit 3.2 to the Registrant's Current Report on Form 8-K on August 6, 2014 and incorporated herein by reference).
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. §1350.
101	The following materials from Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, formatted in eXtensible Business Reporting Language (XBRL) includes: (i) Condensed Balance Sheets at March 31, 2015 (unaudited) and December 31, 2014, (ii) Condensed Statements of Operations and Comprehensive Loss (unaudited) for the three months ended March 31, 2015 and 2014, (iii) Condensed Statements of Cash Flows (unaudited) for the three months ended March 31, 2015 and 2014, and (iv) Notes to the Condensed Financial Statements.

Exhibit 31.1

CERTIFICATION OF THE CHIEF EXECUTIVE OFFICER

PURSUANT TO

SECURITIES EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A)

I, Thomas W. Chalberg, Jr., Ph.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Avalanche Biotechnologies, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 13, 2015

/s/ Thomas W. Chalberg, Jr., Ph.D.
Thomas W. Chalberg, Jr., Ph.D.
President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION OF THE CHIEF FINANCIAL OFFICER

PURSUANT TO

SECURITIES EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A)

I, Linda C. Bain, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Avalanche Biotechnologies, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting;

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 13, 2015

/s/ Linda C. Bain
Linda C. Bain
Chief Financial Officer
(principal financial and accounting officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Avalanche Biotechnologies, Inc. (the "Company") on Form 10-Q for the fiscal quarter ended March 31, 2015, as filed with the Securities and Exchange Commission (the "Report"), Thomas W. Chalberg, Jr., Ph.D., President and Chief Executive Officer of the Company, and Linda C. Bain, Senior Vice President and Chief Financial Officer of the Company, respectively, do each hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- The information in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 13, 2015

/s/ Thomas W. Chalberg, Jr., Ph.D.
Thomas W. Chalberg, Jr., Ph.D.
President and Chief Executive Officer
(principal executive officer)

/s/ Linda C. Bain
Linda C. Bain
Chief Financial Officer
(principal financial and accounting officer)