Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-160922

SUBJECT TO COMPLETION, DATED MARCH 31, 2011

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated August 13, 2009)

Shares of Common Stock

We are offering shares of our common stock in this offering.

Our common stock is listed on The NASDAQ Global Market under the symbol "AVII." On March 30, 2011, the last reported sale price of our common stock was $1.92 per share.

Investing in our common stock involves significant risks. See "Risk Factors" beginning on page S-6 of this prospectus supplement and page 2 of the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$	$
Underwriting discounts and commissions	$	$
Proceeds to AVI BioPharma (before expenses)	$	$

We estimate the total expenses of this offering, excluding the underwriting discounts and commissions, will be approximately $450,000. We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to a total of additional shares of our common stock at the public offering price per share, less the underwriting discounts and commissions, to cover any over-allotments.

We anticipate that delivery of the shares will be made on or about , 2011, subject to customary closing conditions.

Joint Book-Running Managers

LAZARD CAPITAL MARKETS **PIPER JAFFRAY**

Prospectus supplement dated , 2011.

TABLE OF CONTENTS

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under "Where You Can Find Additional Information" on page S-32 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and the underwriters have not, authorized any other person to provide

you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement , in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all the information you should consider before investing in our common stock pursuant to this prospectus supplement and the accompanying prospectus. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including "Risk Factors" beginning on page S-6 of this prospectus supplement, the financial statements, and related notes, and the other information that we incorporated by reference herein, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2010.

AVI BioPharma, Inc.

Overview

We are a biopharmaceutical company focused on the discovery and development of unique RNA-based therapeutics for the treatment of both rare and infectious diseases. Applying our proprietary, highly-differentiated and innovative platform technologies, we are able to target a broad range of diseases and disorders through distinct RNA-based mechanisms of action. We are primarily focused on rapidly advancing the development of our potentially disease-modifying Duchenne muscular dystrophy drug candidates with the intent to realize the product opportunities of such candidates and provide significant clinical benefits. We are also focused on developing therapeutics for the treatment of infectious diseases. By building on the research under our infectious disease programs funded by the U.S. government and leveraging our highly-differentiated, proprietary technology platforms, we are seeking to further develop our research and development competencies and capabilities and identify additional product candidates. We believe that our organizational capabilities will enable us to achieve these goals and become a leading developer and marketer of RNA-based therapeutics for the treatment of both rare and infectious diseases.

Our highly-differentiated RNA-based technologies work at the most fundamental level of biology and potentially could have a meaningful impact across a broad range of human diseases and disorders. Our lead program focuses on the development of disease modifying therapeutic candidates for Duchenne muscular dystrophy, or DMD, a rare genetic muscle wasting disease caused by the absence of dystrophin, a protein necessary for muscle function. AVI-4658 is our lead therapeutic candidate for DMD and is intended to target a substantial group of individuals with DMD. If we are successful in our development efforts, AVI-4658 will address a severe unmet medical need. We intend to initiate a Phase II trial for AVI-4658 in the first half of 2011 with an objective of entering a pivotal trial in the second half of 2012.

We are also leveraging the capabilities of our RNA-based technology platforms to develop therapeutics for the treatment of infectious diseases. The U.S. Department of Defense, or DoD, has provided significant financial support for the development of therapeutics for Ebola, Marburg, Dengue and influenza. In 2010, we were awarded contracts totaling more than $300 million for the research of select therapeutic candidates. We have attracted DoD's support based in part on our ability to rapidly respond to pathogenic threats by quickly identifying, manufacturing and evaluating novel therapeutic candidates.

We employ our highly-differentiated and innovative RNA-based technology platforms in both our DMD and infectious disease programs. The basis for our novel RNA-based therapeutics is our phosphorodiamidate-linked morpholino oligomer, or PMO, chemistries. By applying our technologies, we are able to target a broad range of diseases and disorders through distinct RNA-based mechanisms of action. Unlike other RNA-based therapeutics, our technologies can be used to selectively up-regulate or down-regulate the production of a target protein, or direct the expression of novel proteins involved in human diseases and disorders. Further, we believe

the charge-neutral nature of our PMO-based molecules may have the potential to reduce untargeted immune modulatory effects often seen in alternative RNA-based technologies, as well as certain other off-target effects as seen in a recent trial. As a result of our significant scientific advances generated over years of research and development, we believe that our highly-differentiated, proprietary and innovative RNA-based technology platforms, based on charge neutral morpholino oligomers, may represent a significant improvement over traditional RNA-based technologies.

Corporate Information

We were incorporated in the State of Oregon on July 22, 1980. Our executive office is located at 3450 Monte Villa Parkway, Suite 101, Bothell, Washington 98021 and our telephone number is (425) 354-5038. We maintain an Internet website at www.avibio.com. We have not incorporated the information on our website by reference into this prospectus supplement, and you should not consider it to be a part of this prospectus supplement.

We carry on our business directly and through our subsidiaries. Throughout this prospectus supplement, unless the context specifies or implies otherwise, the terms “Company,” “AVI BioPharma,” “we,” “us,” and “our” refer to AVI BioPharma, Inc., and its subsidiaries.

The Offering

Common stock offered by us	shares
Over-allotment option	shares
Common stock to be outstanding after this offering	shares
Use of proceeds	We currently intend to use the net proceeds from this offering for general corporate purposes, including research and product development, such as funding clinical trials, pre-clinical studies and otherwise moving product candidates towards commercialization. Please see "Use of Proceeds" on page S-25.
Risk factors	See "Risk Factors" beginning on page S-6 of this prospectus supplement for a discussion of factors that you should read and consider before investing in our securities.
NASDAQ Global Market symbol	AVII

The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 112,352,452 shares outstanding as of December 31, 2010. This number of shares does not include shares subject to the underwriters' over-allotment option and also excludes the following:

- 29,665,441 shares of our common stock reserved for issuance upon the exercise of outstanding warrants as of December 31, 2010 with a weighted average exercise price of $1.58 per share;
- 8,490,055 shares of our common stock issuable upon the exercise of stock options outstanding at December 31, 2010 under our 2002 Equity Incentive Plan;
- 1,771,426 shares of our common stock available as of December 31, 2010, for future issuance under our 2002 Equity Incentive Plan;
- 2,247,049 shares of our common stock added to the total number of shares available for issuance under our 2002 Equity Incentive Plan on January 3, 2011 pursuant to the terms of the 2002 Equity Incentive Plan;
- 650,000 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2011, issued outside of our 2002 Equity Incentive Plan;
- up to approximately 15,000,000 shares of our common stock to be reserved for issuance pursuant to an equity incentive plan that we expect to submit for approval by our shareholders at our 2011 annual general meeting; and
- 800,000 shares of our common stock issuable upon the exercise of a stock option expected to be granted on or about May 1, 2011 to induce the acceptance of employment with us by a chief scientific officer.

We anticipate that our chief executive officer and certain of our directors will purchase shares of our common stock in the offering at the public offering price and on the same terms as the other investors purchasing shares of our common stock in the offering.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Investors should carefully consider the risks described below before deciding whether to invest in our securities. The risks described below are not the only ones we face. If any of the following risks actually occurs, our business, financial condition or results of operations could be adversely affected. In such case, the trading price of our common stock could decline and you could lose all or part of your investment. Our actual results could differ materially from those anticipated in the forward-looking statements made throughout this prospectus as a result of different factors, including the risks we face described below.

Risks Relating to Our Business

Our product candidates are at an early stage of development, and it is possible that none of our product candidates will ever become commercial products.

Our product candidates are in relatively early stages of development. These product candidates will require significant further development, financial resources and personnel to obtain regulatory approval and develop into commercially viable products, if at all. Currently, AVI-4658 is in clinical trials, we have open INDs for AVI-6002 in Ebola and AVI-6003 in Marburg, and the rest of our product candidates are in preclinical development. Our IND for AVI-7100 for the treatment of influenza is currently subject to a clinical hold. Providing the evidence required by the FDA to demonstrate that AVI-7100 is safe to use in humans has delayed, and may continue to delay, our clinical development of AVI-7100. Providing the FDA with additional evidence of the safety of the product will require additional time and resources and may not ultimately result in a lifting of the clinical hold, which would materially limit our ability to develop and commercialize this product candidate. We expect that much of our effort and many of our expenditures over the next several years will be devoted to development activities associated with AVI-4658 in Duchenne muscular dystrophy, or DMD, AVI-6002 in Ebola, AVI-6003 in Marburg and AVI-7100 in influenza. With current resources, we may be restricted or delayed in our ability to develop other clinical and preclinical product candidates.

Our ability to commercialize any of our product candidates, including AVI-4658, depends on first receiving required regulatory approvals, and it is possible that we may never receive regulatory approval for any of our product candidates based on an inability to adequately demonstrate the safety and effectiveness of our product candidates, lack of funding, changes in the regulatory landscape or other reasons. Even if a product candidate receives regulatory approval, the resulting product may not gain market acceptance among physicians, patients, healthcare payers and the medical community. Assuming that any of our product candidates receives the required regulatory approvals, commercial success will depend on a number of factors, including:

- establishment and demonstration of clinical efficacy and safety to the medical community;
- cost-effectiveness of the product;
- the availability of adequate reimbursement by third parties, including governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers;
- the product's potential advantage over alternative treatment methods;
- whether the product can be produced in commercial quantities at acceptable costs;
- marketing and distribution support for the product; and
- any exclusivities applicable to the product.

Although we have been granted orphan status for two of our product candidates, we are not guaranteed to receive orphan exclusivity based on that status and would not enjoy such exclusivity in the event that another entity could get approval of the same product for the same indication before we receive approval. Furthermore, pediatric exclusivity only attaches if another exclusivity exists for the product, so if no other regulatory exclusivity or patent protection exists for the product once it is approved, we would not receive the benefit of any pediatric exclusivity.

If we are unable to develop and commercialize any of our product candidates, if development is delayed or if sales revenue from any product candidate that receives marketing approval is insufficient, we may never reach sustained profitability.

If we are unable to obtain or maintain required regulatory approvals, we will not be able to commercialize our product candidates, our ability to generate revenue will be materially impaired and our business will not be successful.

The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA in the United States, and other regulatory authorities in other countries, with regulations differing from country to country. Marketing of our product candidates in the United States or foreign countries is not permitted until we obtain marketing approval from the FDA or other foreign regulatory authorities, and we may never receive regulatory approval for the commercial sale of any of our product candidates. Obtaining marketing approval is a lengthy, expensive and uncertain process and approval is never assured. We have never prepared or filed the applications necessary to gain regulatory approvals. Further, the FDA and other foreign regulatory agencies have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any product candidate we develop. In this regard, even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or any other foreign regulatory authority. In addition, the FDA or their advisors may disagree with our interpretations of data from preclinical studies and clinical trials. Regulatory agencies may approve a product candidate for fewer conditions than requested or may grant approval subject to the performance of post-approval studies for a product candidate. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols or other approval strategies 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. Changes in our approval strategies may require additional studies that were not originally planned. Due to these and other factors, such as the fact that a product utilizing our RNA-based technologies has never been approved by any regulatory authority, our current product candidates or any of our other future product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain regulatory approval, which could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

If we receive regulatory approval for our product candidates, we will also be subject to ongoing FDA obligations and oversight, including adverse event reporting requirements, marketing restrictions and potential other post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize such products. The FDA's policies may also change and additional government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States, or abroad. If we are not able to maintain regulatory compliance, we may be subject to civil and criminal penalties, we may not be permitted to market our products and our business could suffer. Any delay in, or failure to, receive or maintain regulatory approval for any of our product candidates could harm our business and prevent us from ever

generating meaningful revenues or achieving profitability. We will need to obtain regulatory approval from authorities in foreign countries to market our product candidates in those countries. We have not filed for regulatory approval to market our product candidates in any foreign jurisdiction. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. If we fail to obtain approvals from foreign jurisdictions, the geographic market for our product candidates would be limited.

Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy of our product candidates, which could prevent or significantly delay their regulatory approval.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive preclinical and clinical studies, that the product candidate is safe and effective in humans. Ongoing and future clinical trials of our product candidates may not show sufficient safety or efficacy to obtain regulatory approvals.

Phase I clinical trials generally are not designed to test the efficacy of a product candidate but rather are designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the product candidate's side effects at various doses and dosing schedules in healthy volunteers. Delays in establishing the appropriate dosage levels can lead to delays in the overall clinical development of a product candidate. As of the date of this prospectus supplement, we do not believe that we have identified a consistently effective dose of AVI-4658 for individuals with DMD. We are expeditiously moving to start a U.S.-based clinical trial for AVI-4658 at higher doses in the first half of 2011 to further explore and identify a more consistently effective dose that may be more appropriate for future clinical trials and that can serve as a basis for approval by governmental regulatory authorities; however, we cannot assure you that these efforts will be successful. If a consistently effective dose is found in the U.S. based clinical trial, we will expect to engage in discussions with regulatory authorities about the design and subsequent execution of any further studies which may be required. Regulatory authorities might require more extensive clinical trials than anticipated and conforming to any guidance regulatory authorities provide does not guarantee receipt of marketing approval, even if we believe our clinical trials are successful. Such additional clinical trials might include an open label "extension study" for all participants who have previously received AVI-4658, as well as other participants (e.g., non-ambulatory participants) and any additional placebo-controlled "pivotal" study or studies. If we are not able to establish an optimal dosage in this trial we may need to conduct additional dose-ranging trials before conducting our pivotal trials of the product.

Furthermore, success in preclinical and early clinical trials does not ensure that later larger-scale trials will be successful nor does it predict final results. Acceptable results in early trials may not be reproduced in later trials. For example, pivotal trials for AVI-4658 and AVI-7100 will likely involve a larger number of participants to achieve statistical significance, will be expensive and will take a substantial amount of time to complete. As a result, we may conduct lengthy and expensive clinical trials of our product candidates, only to learn that the product candidate is not an effective treatment or is not superior to existing approved therapies, or has an unacceptable safety profile, which could prevent or significantly delay regulatory approval for such product candidate.

The Animal Rule is a new and seldom-used approach to seeking approval of a new drug and may not be a viable pathway for seeking approval of our infectious disease product candidates.

We plan to develop the therapeutic product candidates to treat Ebola and Marburg viruses in the United States using the Animal Rule mechanism. There is no guarantee that the FDA will agree to this approach to the development of our infectious disease product candidates, and if they do not we will have to take a more traditional approach to the development of these products, which may not be possible given ethical considerations and other limitations associated with these deadly diseases. Pursuant to the Animal Rule, the sponsor of a drug product must demonstrate efficacy in humans through animal models. No animal model is established as predicting human outcomes in the prevention or treatment of any filovirus disease. We have yet to demonstrate the predictive value of our animal studies to the FDA's satisfaction. If we fail to do so, we will have to demonstrate efficacy of AVI-6002 and AVI-6003 through adequate well-controlled trials in humans in order to

obtain regulatory approval of these products in the United States, which will greatly add to the time and expense required to commercialize these products. Furthermore, the Animal Rule mechanism has become available only relatively recently and has been infrequently used. We do not have any experience successfully navigating this approach to drug approval. The Animal Rule approach has yet to be well tested generally and is currently under evaluation by the FDA. Even if the Animal Rule represents a viable approach to seeking approval of these products, it may present challenges for gaining final regulatory approval for these product candidates, including an extended timeline to approval and less predictable study requirements.

We rely on U.S. government contracts to support several important research and development programs and substantially all of our revenue. If the U.S. government fails to fund such programs on a timely basis or at all, or such contracts are terminated, the results of our operations would be materially and adversely affected.

We rely on U.S. government contracts and awards to fund several of our development programs, including those for the Ebola, Marburg and influenza viruses and for substantially all of our current revenue.

The funding of U.S. government programs is subject to Congressional appropriations. Congress generally appropriates funds on a fiscal year basis even though a program may extend over several fiscal years. Consequently, programs are often only partially funded initially and additional funds are committed only as Congress makes further appropriations. If appropriations for one of our programs become unavailable or are reduced or delayed, our contracts may be terminated or adjusted by the government, which could have a negative impact on our future revenue under such contract or subcontract. From time to time, when a formal appropriation bill has not been signed into law before the end of the U.S. government's fiscal year, Congress may pass a continuing resolution that authorizes agencies of the U.S. government to continue to operate, generally at the same funding levels from the prior year, but does not authorize new spending initiatives, during a certain period. During such a period, or until the regular appropriation bills are passed, delays can occur in government procurement due to lack of funding and such delays can affect our operations during the period of delay.

In addition, U.S. government contracts generally also permit the government to terminate the contract, in whole or in part, without prior notice, at the government's convenience or for default based on performance. If one of our contracts is terminated for convenience, we would generally be entitled to payments for our allowable costs and would receive some allowance for profit on the work performed. If one of our contracts is terminated for default, we would generally be entitled to payments for our work that has been completed to that point. A termination arising out of our default could expose us to liability and have a negative impact on our ability to obtain future contracts.

The termination of one or more of these government contracts, whether due to lack of funding, for convenience, or otherwise, or the occurrence of delays or product failures in connection with one or more of these contracts, could negatively impact our financial condition. Furthermore, we can give no assurance that we would be able to procure new U.S. government contracts to offset the revenue lost as a result of termination of any of our existing contracts. Even if our contracts are not terminated and are completed, there is no assurance that we will receive future government contracts.

Our U.S. government contracts may be terminated and we may be liable for penalties under a variety of procurement rules and regulations and changes in government regulations or practices could adversely affect our profitability, cash balances or growth prospects.

We must comply with laws and regulations relating to the formation, administration and performance of U.S. government contracts, which affect how we do business with our customers. Such laws and regulations may potentially impose added costs on our business and our failure to comply with them may lead to penalties and the termination of our U.S. government contracts. Some significant regulations that affect us include:

- the Federal Acquisition Regulation and supplements, which regulate the formation, administration and performance of U.S. government contracts;

- the Truth in Negotiations Act, which requires certification and disclosure of cost and pricing data in connection with contract negotiations; and
- the Cost Accounting Standards, which impose accounting requirements that govern our right to reimbursement under certain cost-based government contracts.

Our contracts with the U.S. government are subject to periodic review and investigation. If such a review or investigation identifies improper or illegal activities, we may be subject to civil or criminal penalties or administrative sanctions, including the termination of contracts, forfeiture of profits, the triggering of price reduction clauses, suspension of payments, fines and suspension or debarment from doing business with U.S. government agencies. We could also suffer harm to our reputation if allegations of impropriety were made against us, which would impair our ability to win awards of contracts in the future or receive renewals of existing contracts.

In addition, U.S. government agencies routinely audit and review their contractors' performance on contracts, cost structure, pricing practices and compliance with applicable laws, regulations and standards. They also review the adequacy of, and a contractor's compliance with, its internal control systems and policies, including the contractor's purchasing, property, estimating, compensation and management information systems. Such audits may result in adjustments to our contract costs, and any costs found to be improperly allocated will not be reimbursed. We have recorded contract revenues for the periods presented in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010 and this prospectus supplement based upon costs we expect to realize upon final audit; however, we do not know the outcome of any future audits and adjustments and, if future audit adjustments exceed our estimates, our results of operations could be adversely affected. Additionally, we may be required to enter into agreements and subcontracts with third parties, including suppliers, consultants and other third party contractors in order to satisfy our contractual obligations pursuant to our agreements with the U.S. government. Negotiating and entering into such arrangements can be time-consuming and we may not be able to reach agreement with such third parties. Any such agreement also has to be compliant with the terms of our government grants. Any delay or inability to enter into such arrangements or entering into such arrangements in a manner that is non-compliant with the terms of our grants, may result in violations of our contracts with the U.S. government.

Clinical trials for our product candidates are expensive and time consuming, may take longer than we expect or may not be completed at all, and their outcomes are uncertain.

We have completed a Phase Ib/II clinical trial for AVI-4658 in the UK and announced results in October 2010. We expect to commence additional trials of AVI-4658 and other product candidates in the future, including the initiation of a Phase II trial in AVI-4658 in the first half of 2011. Each of our clinical trials requires the investment of substantial planning, expense and time and the timing of the commencement, continuation and completion of these clinical trials may be subject to significant delays relating to various causes, including scheduling conflicts with participating clinicians and clinical institutions, difficulties in identifying and enrolling participants who meet trial eligibility criteria, failure of participants to complete the clinical trial, delay or failure to obtain IRB or regulatory approval to conduct a clinical trial at a prospective site, unexpected adverse events and shortages of available drug supply. Participant enrollment is a function of many factors, including the size of the relevant population, the proximity of participants to clinical sites, the eligibility criteria for the trial, the existence of competing clinical trials and the availability of alternative or new treatments. We depend on medical institutions and clinical research organizations, or CROs, to conduct our clinical trials in compliance with Good Clinical Practice, or GCP, and to the extent they fail to enroll participants for our clinical trials, fail to conduct the study to GCP standards or are delayed for a significant time in the execution of our trials, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business. In addition, we conduct clinical trials in foreign countries which may subject us to further delays and expenses as a result of increased drug shipment costs, additional regulatory requirements and the engagement of foreign CROs, as well as expose us to risks associated with less experienced clinical investigators who are unknown to the FDA,

and different standards of medical care. Foreign currency transactions insofar as changes in the relative value of the U.S. dollar to the foreign currency where the trial is being conducted may impact our actual costs. In addition, for some programs (e.g., DMD and Ebola and Marburg infections) there are currently no approved drugs to compare against and an agreement about how to measure efficacy has yet to be reached with the FDA and then demonstrated.

Clinical trials must be conducted in accordance with FDA or other applicable foreign government guidelines and are subject to oversight by the FDA, other foreign governmental agencies and IRBs at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced under cGMP and other requirements in foreign countries, and may require large numbers of participants. The FDA or other foreign governmental agencies or we ourselves could delay, suspend or halt our clinical trials of a product candidate for numerous reasons, including:

- deficiencies in the trial design;
- deficiencies in the conduct of the clinical trial, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- deficiencies in the clinical trial operations or trial sites resulting in the imposition of a clinical hold;
- the product candidate may have unforeseen adverse side effects, including fatalities, or a determination may be made that a clinical trial presents unacceptable health risks;
- the time required to determine whether the product candidate is effective may be longer than expected;
- fatalities or other adverse events arising during a clinical trial that may not be related to clinical trial treatments;
- the product candidate may appear to be no more effective than current therapies;
- the quality or stability of the product candidate may fall below acceptable standards;
- our inability to produce or obtain sufficient quantities of the product candidate to complete the trials;
- our inability to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- our inability to obtain IRB approval to conduct a clinical trial at a prospective site;
- our inability to obtain regulatory approval to conduct a clinical trial;
- lack of adequate funding to continue the clinical trial, including the occurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;
- our inability to recruit and enroll individuals to participate in clinical trials for reasons including competition from other clinical trial programs for the same or similar indications; or
- our inability to retain participants who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up.

In addition, we may experience significant setbacks in advanced clinical trials, even after promising results in earlier trials, such as unexpected adverse events that occur when our product candidates are combined with other therapies and drugs or given to larger populations, which often occur in later-stage clinical trials. In addition, clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Also, patient advocacy groups and parents of trial participants may demand additional clinical trials or continued access to drug even if our interpretation of clinical results received thus far leads us to determine that additional clinical trials or continued access are unwarranted. Any disagreement with patient advocacy groups or parents of trial participants may require management's time and attention and may result in legal proceedings being instituted against us, which could be expensive, time-consuming and distracting, and may result in delay of the program. Negative or inconclusive results or adverse medical events, including participant fatalities that may be attributable to our product candidates, during a clinical trial may necessitate it to be redesigned, repeated or terminated. Further, some of our clinical trials may be overseen by an independent data safety monitoring board, or DSMB, and the DSMB may determine to delay or suspend one or more of these trials due to safety or futility findings based on events occurring during a clinical trial.

We have incurred net losses since our inception and we may not achieve or sustain profitability.

We incurred a net loss of $32.2 million for the year ended December 31, 2010 and $25.2 million for the year ended December 31, 2009. As of December 31, 2010, our accumulated deficit was $307.6 million. Our losses have resulted principally from expenses incurred in research and development of our technology and products and from general and administrative expenses that we have incurred while building our business infrastructure. We expect to continue to incur significant operating losses in the future as we continue our research and development efforts and seek to obtain regulatory approval of our products. Our ability to achieve profitability depends on our ability to raise additional capital, partner one or more programs, complete development of our products, obtain regulatory approvals and market our products. It is uncertain when, if ever, we will become profitable.

We will need additional funds to conduct our planned research and development efforts. If we fail to continue to attract significant capital or fail to enter into strategic relationships, we may be unable to continue to develop our product candidates.

We will require additional capital from time to time in the future in order to continue the development of product candidates in our pipeline and to expand our product portfolio. The actual amount of funds that we will need will be determined by many factors, some of which are beyond our control. These factors include the success of our research and development efforts, the status of our pre-clinical and clinical testing, costs relating to securing regulatory approvals and the costs and timing of obtaining new patent rights, regulatory changes and competitive and technological developments in the market. An unforeseen change in these factors, or others, might increase our need for additional capital.

We would expect to seek additional financing from the sale and issuance of equity or debt securities, and we cannot predict that financing will be available when and as we need financing or that, if available, the financing terms will be commercially reasonable. If we are unable to obtain additional financing when and if we require, or on commercially reasonable terms, it would have a material adverse effect on our business and results of operations.

If we are able to consummate such financings, the trading price of our common stock could be adversely affected and/or the terms of such financings may adversely affect the interests of our existing shareholders. To the extent we issue additional equity securities, our existing shareholders could experience substantial dilution in their economic and voting rights. For example, in connection with our December 2007, January 2009 and August 2009 financings, we sold an aggregate of 49.2 million shares of our common stock and issued warrants to purchase an additional 29.7 million shares of our common stock.

Further, we may also enter into relationships with pharmaceutical or biotechnology companies to perform research and development with respect to our RNA-based technologies, research programs or to conduct clinical trials and to market our product candidates. We currently do not have a strategic relationship with a third party to perform research or development using our RNA-based technologies or assist us in funding the continued development and commercialization of any of our programs or drug candidates other than that with the U.S. government. If we are unable to enter into partnerships or strategic relationships with respect to our technologies or any of our programs or drug candidates on favorable terms it may impede our ability to discover, develop and commercialize product candidates.

We currently rely on third-party manufacturers and other third parties for production of our drug products and our dependence on these manufacturers may impair the advancement of our research and development programs and the development of our product candidates.

We do not currently have the internal ability to manufacture the product candidates that we need to conduct our clinical trials and we rely upon a limited number of manufacturers to supply our product candidates. We may also need to rely on manufacturers for the production of our product candidates to support our research and development programs. In addition, we rely on other third parties to perform additional steps in the manufacturing process, including filling and labeling of vials and storage of our product candidates. For the foreseeable future, we expect to continue to rely on contract manufacturers and other third parties to produce, fill vials and store sufficient quantities of our product candidates for use in our research and development programs and clinical trials. For example, for our Ebola and Marburg hemorrhagic fever virus development programs, we have entered into supply agreements with two multinational manufacturing firms for the production of the API for Ebola and Marburg therapeutics. There is a limited number of companies that can produce PMO in the quantities and with the quality and purity that we require for our development efforts. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business.

Our product candidates require precise high-quality manufacturing. The failure to achieve and maintain high quality standards, including failure to detect or control anticipated or unanticipated manufacturing errors could result in patient injury or death or product recalls. Contract drug manufacturers often encounter difficulties involving production yields, quality control and quality assurance and shortages of qualified personnel. If our contract manufacturers or other third parties fail to deliver our product candidates for our research and development programs and for clinical use on a timely basis, with sufficient quality, and at commercially reasonable prices, and we fail to find replacement manufacturers or to develop our own manufacturing capabilities, we may be required to delay or suspend clinical trials, research and development programs or otherwise discontinue development and production of our product candidates. In addition, we depend on outside vendors for the supply of raw materials used to produce our product candidates. If the third-party suppliers were to cease production or otherwise fail to supply us with quality raw materials and we are unable to contract on acceptable terms for these raw materials with alternative suppliers, our ability to have our product candidates manufactured and to conduct preclinical testing and clinical trials of our product candidates would be adversely affected.

We do not yet have all of the agreements necessary for the supply of our product candidates in quantities sufficient for commercial sale and we may not be able to establish or maintain sufficient commercial manufacturing arrangements on commercially reasonable terms. Securing commercial quantities of our product candidates from contract manufacturers will require us to commit significant capital and resources. We may also be required to enter into long-term manufacturing agreements that contain exclusivity provisions and/or substantial termination penalties. In addition, contract manufacturers have a limited number of facilities in which our product candidates can be produced and any interruption of the operation of those facilities due to events such as equipment malfunction or failure or damage to the facility by natural disasters could result in the cancellation of shipments, loss of product in the manufacturing process or a shortfall in available product candidates.

Our contract manufacturers are required to produce our clinical product candidates under current Good Manufacturing Practice, or cGMP, conditions in order to meet acceptable standards for our clinical trials. If such standards change, the ability of contract manufacturers to produce our product candidates on the schedule we require for our clinical trials may be affected. In addition, contract manufacturers may not perform their obligations under their agreements with us or may discontinue their business before the time required by us to successfully produce and market our product candidates. We and our contract manufacturers are subject to periodic unannounced inspection by the FDA and corresponding state and foreign authorities to ensure strict compliance with cGMP and other applicable government regulations and corresponding foreign standards. We do not have control over a third-party manufacturer's compliance with these regulations and standards. Any difficulties or delays in our contractors' manufacturing and supply of product candidates or any failure of our contractors to maintain compliance with the applicable regulations and standards could increase our costs, cause us to lose revenue, make us postpone or cancel clinical trials, prevent or delay regulatory approval by the FDA and corresponding state and foreign authorities, prevent the import and/or export of our product candidates, or cause our products to be recalled or withdrawn.

We may not be able to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing resulting approved drug products, if any.

To date, our product candidates have been manufactured in small quantities for preclinical studies and early stage clinical trials. In order to conduct larger or late-stage scale clinical trials for a product candidate and for commercialization of the resulting drug product if that product candidate is approved for sale, we will need to manufacture it in larger quantities. We may not be able to successfully increase the manufacturing capacity for any of our product candidates, whether in collaboration with third-party manufacturers or on our own, in a timely or cost-effective manner or at all. If a contract manufacturer makes improvements in the manufacturing process for our product candidates, we may not own, or may have to share, the intellectual property rights to those improvements. Significant scale-up of manufacturing may require additional validation studies, which are costly and which the FDA must review and approve. In addition, quality issues may arise during those scale-up activities because of the inherent properties of a product candidate itself or of a product candidate in combination with other components added during the manufacturing and packaging process, or during shipping and storage of the finished product or active pharmaceutical ingredients. If we are unable to successfully scale-up manufacture of any of our product candidates in sufficient quality and quantity, the development of that product candidate and regulatory approval or commercial launch for any resulting drug products may be delayed or there may be a shortage in supply, which could significantly harm our business.

We rely on third parties to provide services in connection with our preclinical and clinical development programs. The inadequate performance by or loss of any of these service providers could affect our product candidate development.

Several third parties provide services in connection with our preclinical and clinical development programs, including in vitro and in vivo studies, assay and reagent development, immunohistochemistry, toxicology, pharmacokinetics, clinical assessments, data monitoring and management and statistical analysis and other outsourced activities. If these service providers do not adequately perform the services for which we have contracted or cease to continue operations and we are not able to quickly find a replacement provider or we lose information or items associated with our product candidates, our development programs may be delayed.

Our RNA-based, or antisense, technology has not been incorporated into a commercial product and is still at a relatively early stage of development.

Our RNA-based platforms, utilizing proprietary antisense technology, have not been incorporated into a commercial product and are still at a relatively early stage of development. This antisense technology is used in all of our therapeutic candidates, including AVI-4658. We are conducting toxicology, pharmacology,

pharmacokinetics and other preclinical studies and, although we have initiated clinical trials for AVI-4658, additional preclinical studies may be required for AVI-4658 and before other product candidates enter human clinical trials. For example, we noted unexpected toxicology findings in the kidney as part of our series of preclinical studies for AVI-5038, our preclinical PPMO drug candidate for DMD that is based on a different chemistry, derived from the PMO chemistry used in AVI-4658. Based on those findings, we conducted additional preclinical work to help clarify the therapeutic index of AVI-5038, but have not yet alleviated the toxicity problem. In addition, preclinical models to study participant toxicity and activity of compounds are not necessarily predictive of toxicity or efficacy of these compounds in the treatment of human disease and there may be substantially different results in clinical trials from the results obtained in preclinical studies. Any failures or setbacks utilizing our antisense technology, including adverse effects resulting from the use of this technology in humans, could have a detrimental impact on our internal product candidate pipeline and our ability to maintain and/or enter into new corporate collaborations regarding these technologies, which would negatively affect our business and financial position.

We intend to increase the size of our workforce and if we fail to manage our growth effectively, our growth prospects and operating results could be adversely affected.

Our ability to perform our U.S. government contracts, growth prospects and operating results depend on highly-skilled personnel to conduct research and product development activities and we intend to recruit, hire and retain additional personnel in the near term. Competition for qualified personnel in our industry, particularly those with experience with either rare or infectious diseases that we target, or may target in the future, is intense. In addition, we expect to meet some of our short-term personnel needs by engaging contractors who may be difficult to retain if they are offered permanent positions with other companies. If we are unable to attract, assimilate or retain such personnel or manage our growth effectively, our continued growth, expansion and ability to advance our proprietary programs and perform our U.S. government contracts would be adversely affected.

We rely on highly skilled personnel, and if we are unable to retain or motivate key personnel or hire qualified personnel, our operations may be adversely affected.

Our operations and our ability to execute our business strategy are highly dependent on the efforts of our executive management team. In April 2010, our chief executive officer and president resigned in connection with the settlement with a group of our shareholders. Following his departure, our board of directors appointed J. David Boyle II, our chief financial officer, to serve as interim chief executive officer and president. In December 2010, our board of directors appointed Christopher Garabedian, a member of the board of directors, to serve as the president and chief executive officer beginning in January 2011. In connection with Mr. Garabedian's appointment, Mr. Boyle returned to the chief financial officer position. If the transition in executive leadership is not smooth, the resulting disruption could negatively affect our operations and impede our ability to execute our strategic plan. In addition, although the members of our senior management team have employment agreements with us, these agreements may not provide sufficient incentives for these officers to continue employment with us. The loss of one or more of the members of our senior management team could adversely affect our operations.

Recent changes in our executive leadership and board of directors and any similar changes in the future may serve as a significant distraction for our management.

As previously disclosed on April 20, 2010, we entered into a settlement agreement with a shareholder group that had sought a special meeting of our shareholders to replace certain members of our board of directors. In connection with such settlement agreement, among other things, we experienced the change in our executive leadership described above and our board of directors underwent significant change. Such changes, or any other future changes in the executive leadership of the Company, may disrupt our operations as our Company adjusts to the reallocation of responsibilities and assimilates new leadership and, potentially, differing perspectives on

our strategic direction. The dispute with the shareholder group required the expenditure of significant time and resources by us and if we are involved in a similar dispute in the future, we may incur significant additional expenditures and it may be a significant distraction for our management and employees.

Asserting, defending and maintaining our intellectual property rights could be challenging and costly, and our failure to do so could harm our ability to compete and impair the outcome of our operations. The pharmaceutical, biotechnology and academic environments are highly competitive and competing intellectual property could limit our ability to protect our products.

Our success will depend in significant part on our existing 189 patents (domestic and foreign) issued or licensed to us and 181 (domestic and foreign) pending patent applications and our ability to obtain additional patents and licenses in the future. We license patents from other parties for certain complementary technologies.

We cannot be certain that pending patent applications will result in patents being issued in the United States or foreign countries. In addition, the patents that have been or will be issued may not afford meaningful protection for our technology and products. Competitors may develop products similar to ours that do not conflict with our patents. Pharmaceutical research and development is highly competitive; others may file patents first that cover our products or technology. We are aware of a European patent to which Prosensa has rights that may provide the basis for Prosensa or other parties that have rights to the patent to assert that our drug AVI-4658 infringes on such patent. We are currently opposing this patent in the Opposition Division of the European Patent Office and believe that we may be able to invalidate some or all of the claims in this patent. Final resolution of this opposition proceeding may take a number of years. Because this proceeding is ongoing, the outcome cannot be predicted or determined as of the date of this prospectus supplement.

Our success will also depend partly on our ability to operate without infringing upon the proprietary rights of others as well as our ability to prevent others from infringing on our proprietary rights. We may be required at times to take legal action to protect our proprietary rights and, despite our best efforts, we may be sued for infringing on the patent rights of others. We have not received any communications or other indications from owners of related patents or others that such persons believe our products or technology may infringe on their patents. Patent litigation is costly and, even if we prevail, the cost of such litigation could adversely affect our financial condition. If we do not prevail, in addition to any damages we might have to pay, we could be required to stop the infringing activity or obtain a license. If any patent related to our products or technology issues, and if our activities are determined to be covered by such a patent, we cannot assure you that we will be able to obtain or maintain a license, which could have a material adverse effect on our business, financial condition, operating results and ability to obtain and/or maintain our strategic business relationships.

Others may challenge our patents and, as a result, our patents could be narrowed or invalidated. The patent position of pharmaceutical and biotechnology firms, as well as academia, is generally highly uncertain, involves complex legal and factual questions, and has recently been the subject of much litigation. No consistent policy has emerged from the U.S. Patent and Trademark Office, or USPTO, or the courts regarding the breadth of claims allowed or the degree of protection afforded under biotechnology patents. In addition, there is a substantial backlog of pharmaceutical and biotechnology patent applications at the USPTO and the approval or rejection of patents may take several years.

To help protect our proprietary rights in unpatented trade secrets, we require our employees, consultants and advisors to execute confidentiality agreements and invention assignment agreements. However, such agreements may not provide us with adequate protection if confidential information is used or disclosed improperly. In addition, in some situations these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors have prior employment or consulting relationships. Further, others may independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets.

Our research collaborators may publish data and information to which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information may be impaired.

We face intense competition and rapid technological change, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. We are aware of many pharmaceutical and biotechnology companies that are actively engaged in research and development in areas related to antisense technology and other RNA technologies or that are developing alternative approaches to or therapeutics for the disease indications on which we are focused. Some of these competitors are developing or testing product candidates that now, or may in the future, compete directly with our product candidates. For example, we believe that companies including Alnylam Pharmaceuticals, Isis Pharmaceuticals, and Santaris share a focus on RNA-based drug discovery and development. Competitors with respect to our exon skipping DMD program, or AVI-4658, include Prosensa and GlaxoSmithKline, or GSK, and other companies such as Acceleron have also been working on DMD programs.

A European based clinical trial evaluating the systemic administration of the Prosensa/GSK lead DMD drug candidate started several months before the start of our similar clinical trial, although the full biological results from this trial have yet to be made publically available. The Prosensa/GSK drug candidate may, or may not, prove to be safer or more efficacious than our product candidate and it could gain marketing approval before our product candidate. This might affect our ability to successfully complete a clinical development program or market AVI-4658 once approved. This competition may also extend to other exon skipping drugs for DMD limiting our ability to gain market share. We also face significant competition with respect to our influenza program from many different companies, including large biopharmaceutical companies that have both marketed products like Tamiflu® and other products in various stages of development.

Other potential competitors include large, fully integrated pharmaceutical companies and more established biotechnology companies that have significantly greater resources and expertise in research and development, manufacturing, testing, obtaining regulatory approvals and marketing. Also, academic institutions, government agencies and other public and private research organizations conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and marketing. It is possible that these competitors will succeed in developing technologies that are more effective than our product candidates or that would render our technology obsolete or noncompetitive. Our competitors may, among other things:

- develop safer or more effective products;
- implement more effective approaches to sales and marketing;
- develop less costly products;
- obtain quicker regulatory approval;
- have access to more manufacturing capacity;
- develop products that are more convenient and easier to administer;
- form more advantageous strategic alliances; or
- establish superior proprietary positions.

We may be subject to clinical trial claims and our insurance may not be adequate to cover damages.

We currently have no products that have been approved for commercial sale; however, the current and future use of our product candidates by us and our corporate collaborators in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made directly by consumers or healthcare providers or indirectly by pharmaceutical companies, our corporate collaborators or others selling such products. We may experience financial losses in the future due to product liability claims. We have obtained limited general commercial liability insurance coverage for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against all losses. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Our operations involve the use of hazardous materials, and we must comply with environmental laws, which can be expensive, and may affect our business and operating results.

Our research and development activities involve the use of hazardous materials, including organic and inorganic solvents and reagents. Accordingly, we are subject to federal, state, and local laws and regulations governing the use, storage, handling, manufacturing, exposure to, and disposal of these hazardous materials. In addition, we are subject to environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens, and the handling of biohazardous materials. Although we believe that our activities conform in all material respects with such environmental laws, there can be no assurance that violations of these laws will not occur in the future as a result of human error, accident, equipment failure, or other causes. Liability under environmental, health and safety laws can be joint and several and without regard to fault or negligence. The failure to comply with past, present, or future laws could result in the imposition of substantial fines and penalties, remediation costs, property damage and personal injury claims, loss of permits or a cessation of operations, and any of these events could harm our business and financial conditions. We expect that our operations will be affected by other new environmental and health and workplace safety laws on an ongoing basis, and although we cannot predict the ultimate impact of any such new laws, they may impose greater compliance costs or result in increased risks or penalties, which could harm our business.

Risks Related to Our Common Stock and this Offering

Provisions of our articles of incorporation, bylaws and Oregon corporate law might deter acquisition bids for us that might be considered favorable and prevent or frustrate any attempt to replace or remove the then current management and board of directors.

Certain provisions of our articles of incorporation and bylaws may make it more difficult for a third party to acquire control of us or effect a change in our board of directors and management. These provisions include:

- classification of our board of directors into two classes, with one class elected each year;
- prohibit cumulative voting of shares in the election of directors;
- prohibit shareholder actions by less than unanimous written consent;
- provide that the board of directors is expressly authorized to make, alter or repeal our bylaws;
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by shareholders at shareholder meetings; and

- the ability of our board of directors to authorize the issuance of undesignated preferred stock, the terms and rights of which may be established and shares of which may be issued without shareholder approval, including rights superior to the rights of the holders of common stock.

In addition, the Oregon Control Share Act and Business Combination Act may limit parties that acquire a significant amount of voting shares from exercising control over us for specific periods of time. These provisions could discourage, delay or prevent a transaction involving a change of control, even if doing so would benefit our shareholders. These provisions also could discourage proxy contests and make it more difficult for shareholders to elect directors of their choosing or cause us to take other corporate actions, such as replacing or removing management or members of our board of directors.

Our stock price is volatile and may fluctuate due to factors beyond our control.

The market prices for, and trading volumes of, securities of biotechnology companies, including our securities, have been historically volatile. The market has from time to time experienced significant price and volume fluctuations unrelated to the operating performance of particular companies. The market price of our common stock may fluctuate significantly due to a variety of factors, including:

- positive or negative results of testing and clinical trials by ourselves, strategic partners, or competitors;
- delays in entering into strategic relationships with respect to development and/or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to our company;
- technological innovations or commercial product introductions by ourselves or competitors;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our products;
- financing or other corporate transactions;
- comments by securities analysts;
- the perception that shares of our common stock may be delisted from The NASDAQ Stock Market; or
- general market conditions in our industry or in the economy as a whole.

In addition, the stock market has recently experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of individual companies. Broad market and industry factors may seriously affect the market price of companies' stock, including ours, regardless of actual operating performance. In addition, in the past, following periods of volatility in the overall market and the market price of a particular company's securities, securities class action litigation has often been instigated against these companies. Such litigation, if instigated against us, could result in substantial costs and a diversion of our management's attention and resources.

Our common stock is listed on The NASDAQ Global Market and we may not be able to maintain that listing, which may make it more difficult for investors to sell shares of our common stock.

Our common stock is listed on The NASDAQ Global Market. The NASDAQ Global Market has several quantitative and qualitative requirements with which companies must comply in order to maintain this listing, including a $1.00 minimum bid price per share and $50 million minimum value of listed securities. In the past our stock price has traded near, and at times below, the $1.00 minimum bid price required for continued listing on NASDAQ. For example, the trading price for our common stock was $0.99 as recently as May 11, 2009. Although NASDAQ in the past has provided relief from the $1.00 minimum bid price requirement as a result of the weakness in the stock market, it may not do so in the future. If we fail to maintain compliance with NASDAQ's listing standards, and our common stock becomes ineligible for listing on The NASDAQ Stock Market the liquidity and price of our common stock would be adversely affected.

If our common stock was delisted, the price of our stock and the ability of our shareholders to trade in our stock would be adversely affected. In addition, we would be subject to a number of restrictions regarding the registration of our stock under U.S. federal securities laws, and we would not be able to allow our employees to exercise their outstanding options, which could adversely affect our business and results of operations. If we are delisted in the future from The NASDAQ Global Market, there may be other negative implications, including the potential loss of confidence by actual or potential collaboration partners, suppliers and employees and the loss of institutional investor interest in our company.

We expect our quarterly operating results to fluctuate in future periods, which may cause our stock price to fluctuate or decline.

Our quarterly operating results have fluctuated in the past, and we believe they will continue to do so in the future. Some of these fluctuations may be more pronounced than they were in the past as a result of the issuance of warrants to purchase 29.7 million shares of our common stock by us in December 2007 and January and August 2009. Each of these warrants is classified as a derivative liability. Accordingly, the fair value of the warrants is recorded on our consolidated balance sheet as a liability, and such fair value is adjusted at each financial reporting date with the adjustment to fair value reflected in our consolidated statement of operations. The fair value of the warrants is determined using the Black-Scholes option valuation model. Fluctuations in the assumptions and factors used in the Black-Scholes model can result in adjustments to the fair value of the warrants reflected on our balance sheet and, therefore, our statement of operations. Due to the classification of such warrants and other factors, quarterly results of operations are difficult to forecast, and period-to-period comparisons of our operating results may not be predictive of future performance. In one or more future quarters, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could decline. In addition, the market price of our common stock may fluctuate or decline regardless of our operating performance.

We may have broad discretion over the use of the proceeds to us from this offering and may apply it to uses that do not improve our operating results or the value of your securities.

We may have broad discretion to use the net proceeds to us from this offering, and investors will be relying solely on the judgment of our board of directors and management regarding the application of these proceeds. Although we expect to use the net proceeds from this offering for general corporate purposes, we have not allocated these net proceeds for specific purposes. Investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately. Our use of the proceeds may not improve our operating results or increase the value of the securities being offered hereby.

A substantial number of shares of common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. A substantial majority of the outstanding shares of

our common stock are, and the shares of common stock sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933.

In addition, in connection with our 2011 annual general meeting of shareholders, we anticipate proposing that our shareholders approve an equity incentive plan providing for the reservation of up to approximately 15,000,000 shares of our common stock.

FORWARD-LOOKING STATEMENTS

Some of the statements contained in this prospectus supplement or incorporated by reference into this prospectus supplement are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and are subject to the safe harbor created by the Securities Litigation Reform Act of 1995. We have based these forward-looking statements largely on our expectations and projections about future events and financial trends affecting the financial condition and/or operating results of our business. Words such as "anticipates," "expects," "intends," "plans," "believes," "seeks," "estimates," the negative of these words, or similar expressions are intended to identify such forward-looking statements. These statements are not guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict; therefore, actual results may differ materially from those expressed or forecasted in any forward-looking statements. The risks and uncertainties include those noted under the heading "Risk Factors" above, in the filings incorporated herein by reference and in the accompanying prospectus. There are important factors that could cause actual results to be substantially different from the results expressed or implied by these forward-looking statements which include, but are not limited to:

- our expectations regarding the development and clinical benefits of our product candidates;
- the results of our research and development efforts and the efficacy of our PMO chemistries and other RNA-based technology;
- our expectations regarding our ability to become a leading developer and marketer of RNA-based therapeutics;
- our expectations regarding the results of pre-clinical and clinical testing of our product candidates;
- our ability to initiate a Phase II clinical trial for AVI-4658 in the first half of 2011 and a pivotal Phase III clinical trial for AVI-4658 in the second half of 2012;
- our ability to initiate Phase I clinical trials in 2011 for our three leading anti-viral product candidates (AVI-6002, AVI-6003 and AVI-7100);
- the receipt of any required approval from the U.S. Food and Drug Administration, or FDA, or other regulatory approval for our products;
- the effect of regulation by FDA and other agencies;
- our intention to introduce new products;
- our expectations regarding the markets for our products;
- acceptance of our products, if introduced, in the marketplace;
- the impact of competitive products, product development, commercialization and technological difficulties;
- our expectations regarding partnering opportunities and other strategic transactions;
- the extent of protection that our patents provide and our pending patent applications may provide, if patents issue from such applications, to our technologies and programs;

- our plans to file additional patent applications to enhance and protect our existing intellectual property portfolio;
- our ability to invalidate some or all of the claims covered by patents issued to competitors;
- our estimates regarding our future revenues, research and development expenses, other expenses, payments to third parties and growth in staffing levels;
- our estimate regarding how long our existing cash, cash equivalents and short-term investments, exclusive of receipt of future proceeds pursuant to our contracts with the U.S. government, will be sufficient to finance our operations;
- our expectations about funding from the government and other sources;
- the adequacy of funds to support our future operations and our future capital needs; and
- other factors set forth above under “Risk Factors” and in the accompanying prospectus, as well as in all filings incorporated by reference into this prospectus supplement.

We do not intend to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. Past financial or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends.

SELECTED FINANCIAL DATA

The consolidated statements of operations data for the years ended December 31, 2008, 2009 and 2010 and the consolidated balance sheets data as of December 31, 2009 and 2010 are derived from our audited consolidated financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010 filed with the SEC on March 15, 2011 and incorporated by reference in this prospectus supplement. The consolidated statements of operations data for the years ended December 31, 2006 and 2007 and the consolidated balance sheets data as of December 31, 2006, 2007 and 2008 are derived from our audited consolidated financial statements not included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010 filed with the SEC on March 15, 2011 and incorporated by reference in this prospectus supplement. Our historical results are not necessarily indicative of the results to be expected in the future. You should read the following selected consolidated financial data below in conjunction with the section captioned "Part II—Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements, related notes and other financial information included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010 filed with the SEC on March 15, 2011 and incorporated by reference in this prospectus supplement. The selected consolidated financial data in this section are not intended to replace the consolidated financial statements and are qualified in their entirety by the consolidated financial statements and related notes included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010 filed with the SEC on March 15, 2011 and incorporated by reference in this prospectus supplement.

	Year Ended December 31,				
	2006	2007	2008	2009	2010
			(in thousands)		
Consolidated statements of operations data:					
Revenues	$ 115	$ 10,985	$ 21,258	$ 17,585	$ 29,420
Research and development	25,346	31,058	27,331	24,396	35,972
General and administrative	7,753	13,035	11,469	8,696	14,382
Acquired in-process research and development	—	—	9,916	—	—
Operating loss	(32,984)	(33,108)	(27,458)	(15,507)	(20,934)
Interest (expense) income, and other net	1,910	984	344	(454)	259
Decrease (increase) on warrant valuation	2,386	4,956	3,161	(9,198)	(11,502)
Net loss	(28,688)	(27,168)	(23,953)	(25,159)	(32,117)
Net loss per share-basic and diluted	$ (0.54)	$ (0.50)	$ (0.34)	$ (0.27)	$ (0.29)

	As of December 31,				
	2006	2007	2008	2009	2010
			(in thousands)		
Consolidated balance sheet data:					
Cash and investments	$ 33,152	$ 25,074	$ 11,474	$ 48,446	$ 33,767
Working capital	25,596	18,959	9,756	17,803	(8,019)
Total assets	40,863	38,638	25,536	60,027	45,976
Shareholders' equity (deficit)	32,519	26,382	15,732	23,630	(2,817)

USE OF PROCEEDS

We estimate that the net proceeds of this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and assuming a total offering size of $28.8 million, will be approximately $26.7 million (or approximately $30.7 million if the underwriters' over-allotment option is exercised in full).

We currently intend to use the net proceeds from this offering for general corporate purposes, including research and product development, such as funding clinical trials, pre-clinical studies and otherwise moving product candidates towards commercialization. The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development and clinical trial efforts, regulatory approvals, competition, our ability to obtain government funding or other non-dilutive financing for the development of certain of our product candidates and our evaluation of opportunities to further accelerate the development efforts for our lead product candidate, AVI-4658. We reserve the right to change the use of proceeds as a result of certain contingencies such as competitive developments, opportunities to acquire technologies or products and other factors. Pending application of the proceeds of sale of the securities, we intend to invest the net proceeds of the sale in short-term, investment-grade, interest-bearing instruments.

DILUTION

Purchasers of common stock offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Our net tangible book value as of December 31, 2010 was approximately $(6,796,397), or approximately $(0.06) per share of common stock. Net tangible book value per share represents the amount of total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of December 31, 2010.

Dilution in net tangible book value per share represents the difference between the amount per unit paid by purchasers of units in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the assumed sale of 15,000,000 shares of common stock in this offering at an assumed public offering price of $1.92 per share, and after deduction of the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2010 would have been approximately $19.9 million, or $0.16 per share of common stock. This represents an immediate increase in net tangible book value of $0.22 per share of common stock to our existing shareholders and an immediate dilution in net tangible book value of $1.76 per share of common stock to investors participating in this offering. The following table illustrates this per share dilution:

Assumed public offering price per share		$ 1.92
Net tangible book value per share as of December 31, 2010	$(0.06)	
Increase per share attributable to this offering	$ 0.22	
As adjusted net tangible book value per share as of December 31, 2010, after giving effect to this offering		$ 0.16
Dilution per share to new investors participating in this offering		$ 1.76

Each $1.00 increase (decrease) in the assumed public offering price of $1.92 per share would increase (decrease) our as adjusted net tangible book value after this offering by approximately $14.1 million, or approximately $0.11 per share, and the dilution per share to new investors by approximately $0.89 per share, assuming that the number of shares offered by us, as set forth above, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering from the assumed number of shares set forth above. An increase of 1,000,000 shares in the number of shares offered by us from the assumed number of shares set forth above would increase our as adjusted net tangible book value after this offering by approximately $1.8 million, or approximately $0.01 per share, and the dilution per share to new investors would be approximately $1.75 per share, assuming that the assumed public offering price remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, a decrease of 1,000,000 shares in the number of shares offered by us from the assumed number of shares set forth above would decrease our as adjusted net tangible book value after this offering by approximately $1.8 million, or approximately $0.02 per share, and the dilution per share to new investors would be approximately $1.78 per share, assuming that the assumed public offering price remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. The information discussed above is illustrative only and will adjust based on the actual public offering price, the actual number of shares that we offer in this offering, and other terms of this offering determined at pricing.

If the underwriters exercise in full their option to purchase 2,250,000 additional shares of common stock at the assumed public offering price of $1.92 per share, the as adjusted net tangible book value after this offering would be $0.18 per share, representing an increase in net tangible book value of $0.25 per share to existing shareholders and immediate dilution in net tangible book value of $1.74 per share to investors participating in this offering at the assumed offering price.

The above table is based on 112,352,452 shares of our common stock outstanding as of December 31, 2010 and excludes, as of December 31, 2010:

- 29,665,441 shares of our common stock reserved for issuance upon the exercise of outstanding warrants with a weighted average exercise price of $1.58 per share;
- 8,490,055 shares of our common stock issuable upon the exercise of stock options outstanding at December 31, 2010 under our 2002 Equity Incentive Plan; and
- 1,771,426 shares of our common stock available as of December 31, 2010, for future issuance under our 2002 Equity Incentive Plan.

2,247,049 shares of our common stock were added to the total number of shares available for issuance under our 2002 Equity Incentive Plan on January 3, 2011 pursuant to the terms of the 2002 Equity Incentive Plan. 650,000 shares of our common stock are issuable upon the exercise of stock options outstanding as of March 31, 2010, issued outside of our 2002 Equity Incentive Plan. Up to approximately 15,000,000 shares of our common stock may be reserved for issuance pursuant to an equity incentive plan that we expect to submit for approval by our shareholders at our 2011 annual general meeting. 800,000 shares of our common stock are issuable upon the exercise of a stock option expected to be granted on or about May 1, 2011 to induce the acceptance of employment with us by a chief scientific officer. To the extent that any options or warrants are exercised, new options are issued under our equity incentive plans, or we otherwise issue additional shares of common stock in the future, there will be further dilution to new investors.

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, Lazard Capital Markets LLC and Piper Jaffray & Co., as underwriters, have each agreed to purchase, and we have agreed to sell to them, the number of shares of our common stock at the public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus supplement as indicated below:

Underwriter	Number of Shares
Lazard Capital Markets LLC	
Piper Jaffray & Co.	
Total	

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus supplement if any such shares are taken.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters may exercise this option at any time and from time to time during the 30-day period from the date of this prospectus supplement. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriters initially propose to offer the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the underwriters.

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of customary legal opinions, letters and certificates.

Commissions and Discounts

The following table summarizes the public offering price, underwriting discounts and commissions and proceeds before expenses to us assuming both no exercise and full exercise of the underwriters' option to purchase additional shares:

		Total	
	Per Share	Without Over-Allotment	With Over-Allotment
Public offering price	$	$	$
Underwriting discounts and commissions			
Proceeds, before expenses, to us			

We anticipate that our chief executive officer and certain of our directors will purchase shares in the offering contemplated by this prospectus supplement at the public offering price and on the same terms as the other investors purchasing shares in the offering; provided that the underwriters will not be entitled to any discounts or commissions with respect to such shares. The immediately preceding table does not give effect to the absence of the discounts and commissions with respect to the shares to be sold to our chief executive officer and directors.

The expenses of the offering, not including the underwriting discounts and commissions, payable by us are estimated to be $450,000, which includes approximately $100,000 that we have agreed to reimburse the underwriters for legal fees incurred in connection with this offering. The aggregate value of all compensation received or to be received by the participating FINRA members does not exceed 8% of the offering proceeds.

The relationship between Lazard Frères & Co. LLC and Lazard Capital Markets LLC is governed by a business alliance agreement between their respective parent companies. Pursuant to such agreement, Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith; however, such referral fee is not in addition to the fee paid by us to Lazard Capital Markets LLC described above.

Indemnification

We and the underwriters have agreed to indemnify each other, and we have also agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement. We have also agreed to contribute to payments the underwriters may be required to make in respect of such liabilities.

No Sales of Similar Securities

We and each of our executive officers and directors, subject to certain exceptions, have agreed with the underwriters not to dispose of or hedge any of our shares of common stock or securities convertible into or exercisable or exchangeable for common stock for 90 days after the date of this prospectus supplement without first obtaining the written consent of the underwriters. The exceptions to the lock-up for executive officers and directors are: (a) transactions relating to shares of common stock or other securities acquired in open market transactions after the completion of the Offering; (b) the transfer of shares of common stock or any securities convertible into or exercisable or exchangeable for common stock (i) to the spouse, domestic partner, parent, child or grandchild of the undersigned or to a trust formed for the benefit of an immediate family member or (ii) by bona fide gift; (c) the transfer of shares of common stock or any securities convertible into shares of common stock to us upon a vesting event of our securities or upon the exercise of options or warrants to purchase our securities, in each case on a "cashless" or "net exercise" basis or to cover tax withholding obligations; (d) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock; and (e) the transfer of shares of common stock or any security convertible into or exercisable or exchangeable for common stock that occurs by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement; each of which is subject to certain conditions set forth in the lock-up agreements with the executive officers and directors. The exceptions to the lock-up for us are: (w) our sale of shares in this offering; (x) the issuance of restricted common stock or options to acquire common stock pursuant to our benefit plans, qualified equity incentive plans or other compensation plans; (y) the issuance of options to induce key personnel to accept employment with our company (whether or not pursuant to a plan), which in the aggregate shall not exceed 2% of our outstanding common stock; and (z) the issuance of common stock pursuant to the valid exercises of options, warrants or rights; each of which is subject to certain conditions set forth in the underwriting agreement. The 90-day "lock-up" period during which we and our executive officers and directors are restricted from engaging in transactions in our common stock or securities convertible into or exercisable or exchangeable for common stock is subject to extension such that, in the event that either (i) during the last 17 days of the "lock-up" period, we issue an earnings or financial results release or material news or a material event relating to us occurs, or (ii) prior to the expiration of the "lock-up" period, we announce that we will release earnings or financial results during the 16-day period beginning on the last day of the "lock-up" period, then in either case the expiration of the "lock-up" period will be extended until the expiration of the 18-day period beginning on the issuance of the earnings or financial results release or the occurrence of the material news or material event, as applicable, unless the underwriters waive, in writing, such an extension.

Price Stabilization, Short Positions

In order to facilitate the offering of our common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. The underwriters must close out any short position by purchasing shares in the open market. A short position may be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchased in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of our common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of our common stock above independent market levels or prevent or slow a decline in the market price of our common stock. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

A prospectus in electronic format may be made available on websites maintained by the underwriters. The underwriters may agree to allocate a number of shares of common stock to other underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters on the same basis as other allocations.

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as "relevant persons"). The shares of common stock are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such common stock will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 or FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to us, and

(b) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

European Economic Area

To the extent that the offer of the common stock is made in any Member State of the European Economic Area that has implemented the Prospectus Directive before the date of publication of a prospectus in relation to the common stock which has been approved by the competent authority in the Member State in accordance with the Prospectus Directive (or, where appropriate, published in accordance with the Prospectus Directive and notified to the competent authority in the Member State in accordance with the Prospectus Directive), the offer (including any offer pursuant to this document) is only addressed to qualified investors in that Member State within the meaning of the Prospectus Directive or has been or will be made otherwise in circumstances that do not require us to publish a prospectus pursuant to the Prospectus Directive.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), each underwriter has represented and agreed that with effect from

and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date") it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities,

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts, or

(c) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive. For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The EEA selling restriction is in addition to any other selling restrictions set out below. In relation to each Relevant Member State, each purchaser of shares of common stock (other than the underwriters) will be deemed to have represented, acknowledged and agreed that it will not make an offer of shares of common stock to the public in any Relevant Member State, except that it may, with effect from and including the date on which the Prospectus Directive is implemented in the Relevant Member State, make an offer of shares of common stock to the public in that Relevant Member State at any time in any circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive, provided that such purchaser agrees that it has not and will not make an offer of any shares of common stock in reliance or purported reliance on Article 3(2)(b) of the Prospectus Directive. For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares of common stock in any Relevant Member State has the same meaning as in the preceding paragraph.

Switzerland

This document does not constitute a prospectus within the meaning of Art. 652a of the Swiss Code of Obligations. The shares of common stock may not be sold directly or indirectly in or into Switzerland except in a manner which will not result in a public offering within the meaning of the Swiss Code of Obligations. Neither this document nor any other offering materials relating to the shares of common stock may be distributed, published or otherwise made available in Switzerland except in a manner which will not constitute a public offer of the shares of common stock in Switzerland.

Listing on The NASDAQ Global Market

Our common shares are traded on The NASDAQ Global Market under the symbol "AVII." The transfer agent for our common shares to be issued in this offering is BNY Mellon Shareowner Services.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by White & Lee LLP, Portland, Oregon. Certain matters will be passed upon for the underwriters by Proskauer Rose LLP, New York, New York.

EXPERTS

The financial statements of AVI BioPharma, Inc. (a development stage company) as of December 31, 2010 and 2009, and for each of the years in the three-year period ended December 31, 2010 and the information included in the cumulative from inception presentations for the period January 1, 2002 to December 31, 2010 (not separately presented), and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2010 have been incorporated by reference herein and in the registration statement in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, and current reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge at our website at http://www.avibio.com under the "SEC FILINGS" caption on the "INVESTOR RELATIONS" page. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not part of this prospectus supplement.

You should rely only on the information provided in, and incorporated by reference in, this prospectus supplement and the prospectus and the registration statement. We have not authorized anyone else to provide you with different information. Our securities are not being offered in any state where the offer is not permitted. The information contained in documents that are incorporated by reference in this prospectus supplement is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the following documents filed with the SEC (excluding those portions of any Form 8-K that are not deemed "filed" pursuant to the General Instructions of Form 8-K):

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2010, filed with the SEC on March 15, 2011;
- portions of our definitive proxy statement on Schedule 14A, filed with the SEC on May 24, 2010 which are incorporated by reference into our Annual Report on Forms 10-K and 10-K/A for the fiscal year ended December 31, 2009, filed with the SEC on March 16, 2010, April 28, 2010 and May 24, 2010;

- our current reports on Form 8-K, as filed with the SEC on December 13, 2010, January 6, 2011 (only with respect to the disclosure under Item 8.01), February 17, 2011, March 14, 2011 (only with respect to the disclosure under Item 8.01), March 28 and March 31, 2011; and

- the description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on May 29, 1997, including any amendments or reports filed for the purposes of updating this description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus supplement is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus supplement, but not delivered with the prospectus supplement, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus supplement incorporates. You should direct written requests to: AVI BioPharma, Inc., 3450 Monte Villa Parkway, Suite 101, Bothell, Washington 98021, or you may call us at (425) 354-5038.

Table of Contents

PROSPECTUS

$125,000,000

AVI BioPharma, Inc.

Common Stock
Preferred Stock
Debt Securities
Warrants to Purchase Common Stock, Preferred Stock or Debt Securities

We may offer and sell from time to time in one or more offerings debt securities, shares of common stock, shares of preferred stock and warrants to purchase common stock, preferred stock or debt securities, up to a total public offering price of $125,000,000.

Our address is 4575 Research Way, Suite 200, Corvallis, Oregon 97333. Our telephone number is (541)753-3635.

Our common stock is quoted on the Nasdaq National Market under the symbol "AVII." The closing sales price of our common stock on the Nasdaq National Market on August 12, 2009 was $2.08 per share.

Each time we sell debt securities, shares of common stock, shares of preferred stock, or warrants to purchase common stock, preferred stock or debt securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described under the heading "Information Incorporated by Reference" before you make your investment decision.

We will sell the securities to or through underwriters or dealers, through agents, or directly to investors, or a combination of these methods. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution."

Investing in our securities stock involves a high degree of risk. See "Risk Factors" beginning on page 2 of this prospectus, as well as in supplements to this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is August 13, 2009.

Table of Contents

TABLE OF CONTENTS

You should rely only on the information contained in this document or to which we have referred you. We have not authorized anyone to provide you with information that is different. This document may only be used where it is legal to sell these securities. The information in this document may only be accurate on the date of this document.

SUMMARY

This summary highlights information about AVI BioPharma, Inc. Because this is a summary, it may not contain all the information you should consider before investing in our securities. You should carefully read this entire prospectus, including the information set forth under "Risk Factors," and the documents incorporated by reference in this prospectus.

AVI BioPharma, Inc.

AVI BioPharma is a biopharmaceutical company specializing in the discovery and development of novel, RNA-based drugs targeting a range of diseases. References in this prospectus to "AVI," the "Company," we," "us" and "our" are to AVI BioPharma, Inc., an Oregon corporation.

As one of the emerging leaders in the fast growing field of RNA therapeutics, AVI has developed and optimized derivatives of its proprietary antisense chemistry (phosphorodiamidate morpholino oligomers or PMOs) that can be designed to target disease mechanisms through distinct mechanisms of action. Unlike other RNA therapeutic approaches, AVI's antisense technology has been used to directly target both messenger RNA (mRNA) and precursor messenger RNA (pre-mRNA) allowing for both down- and up-regulation of targeted genes or proteins. We believe that these broad capabilities give the Company a unique RNA-based technology platform and strong intellectual property position, both of which are the result of advances across several areas of science, including over 20 years of research and development work in chemistry and the Human Genome Project. Our patent estate includes 213 patents (foreign and domestic) issued to or licensed by us and 185 pending patent applications (domestic and foreign).

AVI is leveraging its discovery and development capabilities to build a pipeline of RNA-based therapeutic candidates to develop in collaboration with larger pharmaceutical and biotechnology partners. Current applications of AVI's RNA technology platform include genetic diseases (Duchenne muscular dystrophy), infectious diseases (Ebola and Marburg viruses), cardiovascular disease (restenosis) and other early discovery targets. Several of our antiviral programs, including H1N1 influenza, Ebola, Marburg, Junín and Dengue, have been or are currently funded by the U.S. government, and other governmental and non-governmental funding has supported our other programs.

We are an Oregon corporation headquartered at 4575 SW Research Way, Suite 200, Corvallis, Oregon 97333. Our telephone number is (541) 753-3635. Our website address is *www.avibio.com* . Information contained on our website is not a part of, and is not incorporated into, this prospectus.

This prospectus includes our trademarks and registered trademarks, including NeuGene®, Avicine®, Resten-NG®, Resten-CP™, and Oncomyc-NG™. Each other trademark, trade name or service mark appearing in this prospectus belongs to its holder

RISK FACTORS

Investment in our securities involves a high degree of risk. You should carefully consider the risks described in the section entitled "Risk Factors" in any prospectus supplement as well as in the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, both of which have been filed with the SEC and are incorporated herein by reference in their entirety, as well as other information in this prospectus, any accompanying prospectus supplement, and any other documents or reports incorporated by reference herein before purchasing any of our securities. Each of the risks described in these sections and documents could materially and adversely affect our business, financial condition, results of operations and prospects, and could result in a loss of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus and the information incorporated by reference herein and therein contain forward-looking statements regarding our plans, expectations, estimates and beliefs. Such statements are "forward-looking statements" for purposes of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those discussed in, or implied by, these forward-looking statements. Forward-looking statements are identified by words such as "believe," "anticipate," "expect," "intend," "plan," "will," "may," and other similar expressions. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements are based on current expectations and are not guarantees of future performance. We caution you not to place undue reliance on these statements, which speak only as of the date on which the statement was made. Forward-looking statements in this prospectus supplement and the accompanying prospectus include, but are not necessarily limited to, those relating to:

- our intention to introduce new products,
- receipt of any required FDA or other regulatory approval for our products,
- our expectations about the markets for our products,
- acceptance of our products, when introduced, in the marketplace,
- our expectations about availability of government funding for certain projects,
- our future capital needs,
- results of our research and development efforts, and
- success of our patent applications.

Forward-looking statements are subject to risks and uncertainties, certain of which are beyond our control. Actual results could differ materially from those anticipated as a result of the factors described in "Risk Factors" in the accompanying prospectus and detailed in our other SEC filings, including among others:

- the effect of regulation by the FDA and other governmental agencies,
- delays in obtaining, or our inability to obtain, approval by the FDA or other regulatory authorities for our products,
- research and development efforts, including delays in developing, or the failure to develop, our products,
- uncertainty of government funding for certain projects,
- the development of competing or more effective products by other parties,
- the results of pre-clinical and clinical testing and our ability to conduct these tests,

- uncertainty of market acceptance of our products,
- problems that we may face in manufacturing, marketing, and distributing our products,
- our inability to raise additional capital when needed,
- delays in the issuance of, or the failure to obtain, patents for certain of our products and technologies, and
- problems with important suppliers and business partners.

Because of these risks and uncertainties, the forward-looking events and circumstances discussed in this prospectus and any subsequent prospectus supplement or incorporated by reference might not transpire. Except for our ongoing obligations to disclose material information as required by the federal securities laws, we undertake no obligation to release publicly any revisions to any forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. All of the above factors are difficult to predict, contain uncertainties that may materially affect our actual results and may be beyond our control. New factors emerge from time to time, and it is not possible for our management to predict all of such factors or to assess the effect of each factor on our business.

ABOUT THIS PROSPECTUS

This prospectus is part of a "shelf" registration statement that we have filed with the Securities and Exchange Commission, which we refer to as the "SEC". By using a shelf registration statement, we may issue and sell to the public any part or all of the securities described in the registration statement, at any time and from time to time, in one or more public offerings, up to an aggregate amount of $125,000,000. The exhibits to our registration statement contain the text of certain contracts and other important documents we have summarized in this prospectus, in any prospectus supplement or in the documents incorporated by reference in this prospectus. Since these summaries may not contain all the information that you may find important in deciding whether to purchase the securities we offer, you should review the full text of these documents. The registration statement, the exhibits and the documents incorporated by reference can be obtained from the SEC as indicated under the heading "Where You Can Find More Information."

This prospectus only provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that contains specific information about the terms of those securities. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described below under the heading "Where You Can Find More Information," and "Information Incorporated by Reference."

We may sell the securities to or through underwriters or dealers, through agents, or directly to investors, or a combination of these methods. We and our agents reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. See "Plan of Distribution" below. A prospectus supplement, which we will provide to you each time we offer securities, will provide the names of any underwriters, dealers, or agents involved in the sale of the securities, and any applicable fee, commission, or discount arrangements with them.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information in this prospectus or a prospectus supplement is accurate as of any date other than the date on the front of the document.

RATIO OF EARNINGS TO FIXED CHARGES

We present below the ratio of our earnings to our fixed charges. Earnings consist of net loss plus fixed charges. Fixed charges consist of interest expense, including amortization of debt issuance costs, and that portion of rental expense we believe to be representative of interest.

	Ratio of Earnings to Fixed Charges					
		Year ended December 31,				
	Three months ended March 31, 2009	2008	2007	2006	2005	2004
Ratio of Earnings to Fixed Charges	—	—	—	—	—	—
Coverage deficiency	$ (927)	$(23,953)	$(27,168)	$(28,688)	$(18,206)	$(21,937)

USE OF PROCEEDS

Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of our securities for research and development and general corporate purposes. We may also use a portion of the net proceeds to commercialize our products, or to acquire or invest in businesses, products and technologies that are complementary to our own or provide us with a strategic advantage. We may also issue the securities offered under this prospectus in connection with product license and supply agreements, research collaboration agreements and to our commercial vendors and suppliers in exchange for products and services. Until we use the net proceeds of this offering for the above purposes, we intend to invest the funds in short-term, investment grade, interest-bearing securities. We cannot predict whether the proceeds invested will yield a favorable return.

SECURITIES WE MAY OFFER

We may offer from time to time in one or more offerings debt securities, shares of common stock, shares of preferred stock and warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units consisting of one or more securities. We may offer up to $125,000,000 of securities under this prospectus. If securities are offered as units, we will describe the terms of the units in a prospectus supplement.

DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK

We describe below the common stock and preferred stock we may offer under this prospectus. The terms we summarize below will apply generally to any future common stock or preferred stock that we may offer. We will describe the particular terms of these securities in more detail in a prospectus supplement.

Common Stock

We are authorized to issue 200,000,000 shares of common stock, of which 85,725,709 shares were issued and outstanding as of the date hereof. Each shareholder of record is entitled to one vote for each outstanding share of our common stock owned by that shareholder on every matter properly submitted to the shareholders for their vote. Subject to the satisfaction of the dividend rights of holders of any shares of preferred stock issued hereafter, holders of common stock are entitled to any dividend declared by the board of directors out of funds legally available for this purpose. Subject to the payment of liquidation preferences to holders of any shares of preferred stock issued hereafter, holders of our common stock are entitled to receive, on a pro rata basis, all of our remaining assets available for distribution to the shareholders in the event of our liquidation, dissolution, or winding up. Holders of our common stock do not have any preemptive right to subscribe or purchase additional shares of any class of our capital stock. The preferences, limitations, relative rights and other terms of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Our articles of incorporation allow us to issue, without shareholder approval, preferred stock having rights senior to those of our common stock. Our board is authorized, without further shareholder approval, to issue up to 20,000,000 shares of preferred stock, of which no shares are currently issued and outstanding, in one or more series and to fix and designate the preferences, limitations, relative rights and other terms of the preferred stock, including:

- dividend rights;
- conversion rights;

- voting rights;
- terms of redemption; and
- liquidation preferences.

Our board of directors may fix the number of shares constituting any series of preferred stock and the designations of the series. We will fix the preferences, limitations, relative rights and other terms of the preferred stock of each series by the filing of articles of amendment relating to each series. We will specify the terms of the preferred stock in a prospectus supplement, including:

- the maximum number of shares in the series and the distinctive designation;
- the terms on which dividends will be paid, if any;
- the terms on which the shares may be redeemed, if at all;
- the liquidation preference, if any;
- the terms of any retirement or sinking fund for the purchase or redemption of the shares of the series;
- the terms and conditions, if any, on which the shares of the series will be convertible into, or exchangeable for, shares of any other class or classes of capital stock;
- the voting rights, if any, on the shares of the series; and
- any or all other preferences and relative, participating, operational or other special rights or qualifications, limitations or restrictions of the shares.

We will describe the specific terms of a particular series of preferred stock in the prospectus supplement relating to that series. We urge you to read the applicable articles of amendment and the description in the prospectus supplement. The prospectus supplement will contain a description of the U.S. federal income tax consequences relating to the preferred stock.

Our issuance of preferred stock may have the effect of delaying or preventing a change in control. Our issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of our common stock or could adversely affect the rights and powers, including voting rights, of the holders of our common stock. The issuance of preferred stock could have the effect of decreasing the market price of our common stock.

Transfer Agent

The transfer agent for our common stock is BNY Mellon Shareowner Services, Pittsburgh, Pennsylvania.

DESCRIPTION OF DEBT SECURITIES

We may offer any combination of senior debt securities or subordinated debt securities. Debt securities are secured or unsecured obligations to repay advanced funds. We may issue the senior debt securities and the subordinated debt securities under separate indentures between us, as issuer, and the trustee or trustees identified in the prospectus supplement. We filed the form for each type of indenture as an exhibit to the registration statement of which this prospectus is a part.

We will describe the particular terms of any debt securities we may offer in a prospectus supplement. The following summaries of the debt securities and the indentures are not complete. We urge you to read the indentures and the description of the debt securities included in the prospectus supplement.

General

We may issue debt securities in separate series. We may specify a maximum aggregate principal amount for the debt securities of any series. The debt securities will have terms that are consistent with the indentures. Unless the prospectus supplement indicates otherwise, senior debt securities will be unsecured and unsubordinated obligations and will rank equal with all our other unsecured and unsubordinated debt. We will make payment on our subordinated debt securities only if we have made all payments due under our senior indebtedness, including any outstanding senior debt securities.

The indentures might not limit the amount of other debt that we may incur and might not contain financial or similar restrictive covenants. The indentures might not contain any provision to protect holders of debt securities against a sudden or dramatic decline in our ability to pay our debt.

We will describe the debt securities and the price or prices at which we will offer the debt securities in a prospectus supplement. We will describe:

- the title and form of the debt securities;
- any limit on the aggregate principal amount of the debt securities or the series of which they are a part;
- the person to whom any interest on a debt security of the series will be paid;
- the date or dates on which we must repay the principal;
- the rate or rates at which the debt securities will bear interest, if any, the date or dates from which interest will accrue, and the dates on which we must pay interest;
- if applicable, the duration and terms of the right to extend interest payment periods;
- the place or places where we must pay the principal and any premium or interest on the debt securities;
- the terms and conditions on which we may redeem any debt security, if at all;
- any obligation to redeem or purchase any debt securities, and the terms and conditions on which we must do so;
- the denominations in which we may issue the debt securities;
- the manner in which we will determine the amount of principal of or any premium or interest on the debt securities;
- the currency in which we will pay the principal of and any premium or interest on the debt securities;
- the principal amount of the debt securities that we will pay upon declaration of acceleration of their maturity;
- the amount that will be deemed to be the principal amount for any purpose, including the principal amount that will be due and payable upon any maturity or that will be deemed to be outstanding as of any date;

- if applicable, that the debt securities are defeasible and the terms of such defeasance;
- if applicable, the terms of any right to convert debt securities into, or exchange debt securities for, shares of common stock or other securities or property;
- the subordination provisions that will apply to any subordinated debt securities;
- any addition to or change in the events of default applicable to the debt securities and any change in the right of the trustee or the holders to declare the principal amount of any of the debt securities due and payable; and
- any addition to or change in the covenants in the indentures.

We may sell the debt securities at a substantial discount below their stated principal amount. We will describe U.S. federal income tax considerations, if any, applicable to debt securities sold at an original issue discount in the prospectus supplement. An "original issue discount security" is any debt security sold for less than its face value, and which provides that the holder cannot receive the full face value if maturity is accelerated. We will describe the particular provisions relating to acceleration of the maturity upon the occurrence of an event of default in the prospectus supplement. In addition, we will describe U.S. federal income tax or other considerations applicable to any debt securities that are denominated in a currency or unit other than U.S. dollars in the prospectus supplement.

Conversion and Exchange Rights

If applicable, we will describe the terms on which the debt holder may convert debt securities into or exchange them for common stock or other securities or property in the prospectus supplement. The conversion or exchange may be mandatory or may be at the debt holder's option. We will describe how to calculate the number of shares of common stock or other securities or property that the debt holder will receive upon conversion or exchange.

Subordination of Subordinated Debt Securities

We will pay the indebtedness underlying the subordinated debt securities if we have made all payments due under our senior indebtedness, including any outstanding senior debt securities. If we distribute our assets to creditors upon any dissolution, winding-up, liquidation or reorganization or in bankruptcy, insolvency, receivership or similar proceedings, we must first pay all amounts due or to become due on all senior indebtedness before we pay the principal of, or any premium or interest on, the subordinated debt securities. If an event of default accelerates the subordinated debt securities, we may not make any payment on the subordinated debt securities until we have paid all senior indebtedness or the acceleration is rescinded. If the payment of subordinated debt securities accelerates because of an event of default, we must promptly notify holders of senior indebtedness of the acceleration.

If we experience a bankruptcy, dissolution or reorganization, holders of senior indebtedness may receive more, ratably, and holders of subordinated debt securities may receive less, ratably, than our other creditors. The indenture for subordinated debt securities may not limit our ability to incur additional senior indebtedness.

Form, Exchange and Transfer

We will issue debt securities only in fully registered form, without coupons, and only in denominations of $1,000 and integral multiples thereof. The holder of a debt security may elect, subject to the terms of the indentures and the limitations applicable to global securities, to exchange them for other debt securities of the same series of any authorized denomination and of similar terms and aggregate principal amount.

Holders of debt securities may present them for exchange as provided above or for registration of transfer, duly endorsed or with the form of transfer duly executed, at the office of the transfer agent we designate for that purpose. We will not impose a service charge for any registration of transfer or exchange of debt securities, but

we may require a payment sufficient to cover any tax or other governmental charge payable in connection with the transfer or exchange. We will name the transfer agent in the prospectus supplement. We may designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, but we must maintain a transfer agent in each place in which we will pay on debt securities.

If we redeem the debt securities, we will not be required to issue, register the transfer of or exchange any debt security during a specified period prior to mailing a notice of redemption. We are not required to register the transfer of or exchange any debt security selected for redemption, except the unredeemed portion of the debt security being redeemed.

Global Securities

The debt securities may be represented, in whole or in part, by one or more global securities that will have an aggregate principal amount equal to that of all debt securities of that series. We will deposit each global security with a depositary or a custodian. The global security will bear a legend regarding the restrictions on exchanges and registration of transfer.

No global security may be exchanged in whole or in part for debt securities registered, and no transfer of a global security in whole or in part may be registered, in the name of any person other than the depositary or any nominee or successor of the depositary unless:

- the depositary is unwilling or unable to continue as depositary; or
- the depositary is no longer in good standing under the Securities Exchange Act of 1934, as amended, or the Exchange Act, or other applicable statute or regulation.

The depositary will determine how all securities issued in exchange for a global security will be registered.

As long as the depositary or its nominee is the registered holder of a global security, we will consider the depositary or the nominee to be the sole owner and holder of the global security and the underlying debt securities. Except as stated above, owners of beneficial interests in a global security will not be entitled to have the global security or any debt security registered in their names, will not receive physical delivery of certificated debt securities and will not be considered to be the owners or holders of the global security or underlying debt securities. We will make all payments of principal, premium and interest on a global security to the depositary or its nominee. The laws of some jurisdictions require that some purchasers of securities take physical delivery of such securities in definitive form. These laws may prevent the debt holder from transferring its beneficial interests in a global security.

Only institutions that have accounts with the depositary or its nominee and persons that hold beneficial interests through the depositary or its nominee may own beneficial interests in a global security. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants. The ownership of beneficial interests in a global security will be shown only on, and the transfer of those ownership interests will be effected only through, records maintained by the depositary or any such participant.

The policies and procedures of the depositary may govern payments, transfers, exchanges and others matters relating to beneficial interests in a global security. We and the trustee will assume no responsibility or liability for any aspect of the depositary's or any participant's records relating to, or for payments made on account of, beneficial interests in a global security.

Payment and Paying Agents

Unless we indicate otherwise, we will pay principal and any premium or interest on a debt security to the person in whose name the debt security is registered at the close of business on the regular record date for such interest.

Unless we indicate otherwise, we will pay principal and any premium or interest on the debt securities at the office of our designated paying agent. Unless we indicate otherwise, the corporate trust office of the trustee will be the paying agent for the debt securities.

We will name any other paying agents for the debt securities of a particular series in the prospectus supplement. We may designate additional paying agents, rescind the designation of any paying agent or approve a change in the office through which any paying agent acts, but we must maintain a paying agent in each place of payment for the debt securities.

The paying agent will return to us all money we pay to it for the payment of the principal, premium or interest on any debt security that remains unclaimed for a specified period. Thereafter, the holder may look only to us for payment, as an unsecured general creditor.

Consolidation, Merger and Sale of Assets

Under the terms of the indentures, so long as any securities remain outstanding, we may not consolidate or enter into a share exchange with or merge into any other person, in a transaction in which we are not the surviving corporation, or sell, convey, transfer or lease our properties and assets substantially as an entirety to any person, unless:

- the successor assumes our obligations under the debt securities and the indentures; and
- we meet the other conditions described in the indentures.

Events of Default

Each of the following will constitute an event of default under each indenture:

- our failure to pay the principal of or any premium on any debt security when due;
- our failure to pay any interest on any debt security when due, for more than a specified number of days past the due date;
- our failure to deposit any sinking fund payment when due;
- our failure to perform any covenant or agreement in the indenture that continues for a specified number of days after written notice has been given by the trustee or the holders of a specified percentage in aggregate principal amount of the debt securities of that series;
- certain events of our bankruptcy, insolvency or reorganization; and
- any other event of default specified in the prospectus supplement.

If an event of default occurs and continues, both the trustee and holders of a specified percentage in aggregate principal amount of the outstanding securities of that series may declare the principal amount of the debt securities of that series to be immediately due and payable. The holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul the acceleration if all events of default, other than the nonpayment of accelerated principal, have been cured or waived.

Except for certain duties in case of an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request or direction of any of the holders, unless the holders have offered the trustee reasonable indemnity. If they provide this indemnification, the holders of a majority in aggregate principal amount of the outstanding securities of any series may direct the time, method and place of conducting any

proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

No holder of a debt security of any series may institute any proceeding with respect to the indentures, or for the appointment of a receiver or a trustee, or for any other remedy, unless:

- the holder has previously given the trustee written notice of a continuing event of default;
- the holders of a specified percentage in aggregate principal amount of the outstanding securities of that series have made a written request upon the trustee, and have offered reasonable indemnity to the trustee, to institute the proceeding;
- the trustee has failed to institute the proceeding for a specified period of time after its receipt of the notification; and
- the trustee has not received a direction inconsistent with the request within a specified number of days.

Modification and Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, we and the trustee may change the rights of holders of a series of notes with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, we and the trustee may only make the following changes with the consent of the holder of any outstanding debt securities affected:

- extending the fixed maturity of the series of notes;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption, of any debt securities; or
- reducing the percentage of debt securities the holders of which are required to consent to any amendment.

The holders of a majority in principal amount of the outstanding debt securities of any series may waive any past default under the indenture with respect to debt securities of that series, except a default in the payment of principal, premium or interest on any debt security of that series or in respect of a covenant or provision of the indenture that cannot be amended without each holder's consent.

Except in certain limited circumstances, we may set any day as a record date for the purpose of determining the holders of outstanding debt securities of any series entitled to give or take any direction, notice, consent, waiver or other action under the indentures. In certain limited circumstances, the trustee may set a record date. To be effective, the action must be taken by holders of the requisite principal amount of such debt securities within a specified period following the record date.

Defeasance

We may apply the provisions in the indentures relating to defeasance and discharge of indebtedness, or to defeasance of certain restrictive covenants, to the debt securities of any series. The indentures provide that, upon satisfaction of the requirements described below, we may terminate all of our obligations under the debt securities of any series and the applicable indenture, known as legal defeasance, other than our obligation:

- to maintain a registrar and paying agents and hold moneys for payment in trust;

- to register the transfer or exchange of the notes; and
- to replace mutilated, destroyed, lost or stolen notes.

In addition, we may terminate our obligation to comply with any restrictive covenants under the debt securities of any series or the applicable indenture, known as covenant defeasance.

We may exercise our legal defeasance option even if we have previously exercised our covenant defeasance option. If we exercise either defeasance option, payment of the notes may not be accelerated because of the occurrence of events of default.

To exercise either defeasance option as to debt securities of any series, we must irrevocably deposit in trust with the trustee money and/or obligations backed by the full faith and credit of the U.S. that will provide money in an amount sufficient in the written opinion of a nationally recognized firm of independent public accountants to pay the principal of, premium, if any, and each installment of interest on the debt securities. We may establish this trust only if:

- no event of default has occurred and continues to occur;
- in the case of legal defeasance, we have delivered to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the IRS a ruling or there has been a change in law, which in the opinion of our counsel, provides that holders of the debt securities will not recognize gain or loss for federal income tax purposes as a result of such deposit, defeasance and discharge and will be subject to federal income tax on the same amount, in the same manner and at the same times as would have been the case if such deposit, defeasance and discharge had not occurred;
- in the case of covenant defeasance, we have delivered to the trustee an opinion of counsel to the effect that the holders of the debt securities will not recognize gain or loss for federal income tax purposes as a result of such deposit, defeasance and discharge and will be subject to federal income tax on the same amount, in the same manner and at the same times as would have been the case if such deposit, defeasance and discharge had not occurred; and
- we satisfy other customary conditions precedent described in the applicable indenture.

Notices

We will mail notices to holders of debt securities as indicated in the prospectus supplement.

Title

We may treat the person in whose name a debt security is registered as the absolute owner, whether or not such debt security may be overdue, for the purpose of making payment and for all other purposes.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the state of Oregon.

DESCRIPTION OF WARRANTS

Warrant to Purchase Common Stock or Preferred Stock

The following summarizes the terms of common stock warrants and preferred stock warrants we may issue. We urge you to read the detailed provisions of the stock warrant agreement that we will enter into with a stock warrant agent we select at the time of issue.

General. We may issue stock warrants evidenced by stock warrant certificates under a stock warrant agreement independently or together with any securities we offer by any prospectus supplement. If we offer stock warrants, we will describe the terms of the stock warrants in a prospectus supplement, including:

- the offering price, if any;
- the number of shares of common or preferred stock purchasable upon exercise of one stock warrant and the initial price at which the shares may be purchased upon exercise;
- if applicable, the designation and terms of the preferred stock purchasable upon exercise of the stock warrants;
- the dates on which the right to exercise the stock warrants begins and expires;
- U.S. federal income tax consequences;
- call provisions, if any;
- the currencies in which the offering price and exercise price are payable; and
- if applicable, any antidilution provisions.

Exercise of Stock Warrants. The holder may exercise a stock warrant by surrendering to the stock warrant agent the stock warrant certificate, which indicates the holder's election to exercise all or a portion of the stock warrants evidenced by the certificate. The holder must pay the exercise price by cash or check when the holder surrenders its stock warrant certificate. The stock warrant agent will deliver certificates evidencing duly exercised stock warrants to the transfer agent. Upon receipt of the certificates, the transfer agent will deliver a certificate representing the number of shares of common stock or preferred stock purchased. If the holder exercises fewer than all the stock warrants evidenced by any certificate, the stock warrant agent will deliver a new stock warrant certificate representing the unexercised stock warrants.

No Rights as Shareholders. Holders of stock warrants are not entitled to vote, to consent, to receive dividends or to receive notice as shareholders with respect to any meeting of shareholders, or to exercise any rights whatsoever as shareholders.

Warrants to Purchase Debt Securities

The following summarizes the terms of the debt warrants we may offer. We urge you to read the detailed provisions of the debt warrant agreement that we will enter into with a debt warrant agent we select at the time of issue.

General. We may issue debt warrants evidenced by debt warrant certificates independently or together with any securities offered by any prospectus supplement. If we offer debt warrants, we will describe the terms of the warrants in a prospectus supplement, including:

- the offering price, if any;
- the designation, aggregate principal amount and terms of the debt securities purchasable upon exercise of the warrants and the terms of the indenture under which the debt securities will be issued;
- if applicable, the designation and terms of the debt securities with which the debt warrants are issued and the number of debt warrants issued with each debt security;

- if applicable, the date on and after which the debt warrants and any related securities will be separately transferable;
- the principal amount of debt securities purchasable upon exercise of one debt warrant and the price at which the principal amount of debt securities may be purchased upon exercise;
- the dates on which the right to exercise the debt warrants begins and expires;
- U.S. federal income tax consequences;
- whether the warrants represented by the debt warrant certificates will be issued in registered or bearer form;
- the currencies in which the offering price and exercise price are payable; and
- if applicable, any antidilution provisions.

The holder may exchange debt warrant certificates for new debt warrant certificates of different denominations and may present debt warrant certificates for registration of transfer at the corporate trust office of the debt warrant agent, which we will list in the prospectus supplement. The holder will not have any of the rights of holders of debt securities, except to the extent that the consent of warrantholders may be required for certain modifications of the terms of an indenture or form of the debt security and the series of debt securities issuable upon exercise of the debt warrants. In addition, the holder will not receive payments of principal of and interest, if any, on the debt securities unless the holder exercises its debt warrant.

Exercise of Debt Warrants. The holder may exercise debt warrants by surrendering to the debt warrant agent the debt warrant certificate, with payment in full of the exercise price. Upon the exercise of debt warrants, the debt warrant agent will, as soon as practicable, deliver to the holder the debt securities in authorized denominations in accordance with the holder's instructions and at its sole cost and risk. If the holder exercises fewer than all the debt warrants evidenced by any debt warrant certificate, the agent will deliver to the holder a new debt warrant certificate representing the unexercised debt warrants.

PLAN OF DISTRIBUTION

We may sell the securities through underwriters or dealers, through agents, or directly to one or more purchasers. We will describe the terms of the offering of the securities in a prospectus supplement, including:

- the name or names of any underwriters, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any underwriting discounts and other items constituting underwriters' compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters we name in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If we use underwriters in the sale, they will acquire the securities for their own account and may resell them from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all the securities of the series offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

Securities may also be sold in one or more of the following transactions: (a) block transactions (which may involve crosses) in which a broker-dealer may sell all or a portion of the securities as agent but may position and resell all or a portion of the block as principal to facilitate the transaction; (b) purchases by a broker-dealer as principal and resale by the broker-dealer for its own account pursuant to a prospectus supplement; (c) ordinary brokerage transactions and transactions in which a broker-dealer solicits purchasers; (d) sales "at the market" to or through a market maker or into an existing trading market, on an exchange or otherwise, for securities; and (e) sales in other ways not involving market makers or established trading markets, including direct sales to purchasers. Broker-dealers may also receive compensation from purchasers of the securities which is not expected to exceed that customary in the types of transactions involved.

We may provide agents and underwriters with indemnification against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, or the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to such liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer other than common stock will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment).

LEGAL MATTERS

Unless otherwise specified in the prospectus supplement accompanying this prospectus, Davis Wright Tremaine LLP, 1300 S.W. Fifth Avenue, 23rd Floor, Portland, Oregon 97201, will provide opinions regarding the authorization and validity of the securities. Any underwriters will also be advised about legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

The financial statements of AVI BioPharma, Inc. as of December 31, 2008 and 2007, and for each of the years in the three-year period ended December 31, 2008, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2008 have been incorporated by reference herein and in the registration statement in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public from the SEC's web site at http://www.sec.gov. You may also read and copy any document we file at the SEC's public reference room in Washington, D.C. located at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of any document we file at prescribed rates by writing to the Public Reference Section of the Securities Exchange Commission at that address. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. Information about us, including our SEC filings, is also available on our website at *http://www.avibio.com* ; however, that information is not a part of this prospectus or any accompanying prospectus supplement.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" in this prospectus the information in other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus or a prospectus supplement. We incorporate by reference in this prospectus the documents listed below and any future filings that we may make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, prior to the termination of the offering under this prospectus:

- Annual Report on Form 10-K for the year ended December 31, 2008;
- Quarterly Report on Form 10-Q for the quarter ended June 30, 2009;
- Current Reports on Form 8-K filed on January 30, 2009, January 30, 2009, March 10, 2009, April 1, 2009, May 11, 2009, May 21, 2009, June 2, 2009, June 8, 2009, July 31, 2009, and August 10 and
- The description of our common stock contained in our registration statement on Form 8-A filed on May 29, 1997.

Notwithstanding the foregoing, we are not incorporating any document or information deemed to have been furnished and not filed in accordance with SEC rules. You may obtain a copy of any or all of the documents referred to above which may have been or may be incorporated by reference into this prospectus (excluding certain exhibits to the documents) at no cost to you by writing or telephoning us at the following address:

AVI BioPharma, Inc.
Investor Relations
4575 SW Research Way, Suite 200
Corvallis, OR 97333
Attn: Julie Rathbun
(541) 224-2575

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

LAZARD CAPITAL MARKETS **PIPER JAFFRAY**

, 2011.