ZONAGEN INC
Form S-1
October 20, 2004

As filed with the Securities and Exchange Commission on October 20, 2004
Registration No. 333- l

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

Zonagen, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**72-0233274**	**2834**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*	*(Primary Standard Industrial Classification Code Number)*

2408 Timberloch Dr., Suite B-1

The Woodlands, Texas 77380
(281) 719-3400
(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Joseph S. Podolski

President and Chief Executive Officer
2408 Timberloch Dr., Suite B-1
The Woodlands, Texas 77380
(281) 719-3400
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Jeffrey R. Harder, Esq
Paul D. Aubert, Esq
Winstead Sechrest & Minick P.C.
1450 Lake Robbins Drive, Suite 600
The Woodlands, Texas 77380
(281) 681-5900

Jeffrey S. Marcus, Esq.
Christopher D. Arana, Esq.
Morrison & Foerster LLP
1290 Avenue of the Americas
New York, New York 10104
(212) 468-8000

Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price (2)	Amount of Registration Fee (3)
Common Stock, par value $0.001 per share (1)	$14,840,000	$1,850

(1) This registration statement also relates to rights to purchase shares of Series One Junior Participating Preferred Stock of the registrant attached to the shares of the registrant s common stock issued pursuant to the terms of the registrant s Rights Agreement dated as of September 1, 1999, as amended. Until the occurrence of certain prescribed events, the rights are not exercisable, are evidenced by certificates of the common stock and will be transferred with and only with the common stock. Because no separate consideration is paid for the rights, the registration fee for the rights is included in the registration fee for the common stock.

(2) Estimated solely for purposes of calculating the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended.

(3) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated 1 , 2004.

4,000,000 Shares

ZONAGEN, INC.

Common Stock

We are offering 4,000,000 shares of our common stock. We have granted the underwriter a 30-day option to purchase up to an additional 600,000 shares to cover over-allotments.

Our common stock is quoted on the Nasdaq SmallCap Market under the symbol ZONA and the Pacific Stock Exchange under the symbol ZNG. The last reported sale price of our common stock on the Nasdaq SmallCap Market on October 19, 2004 was $3.71.

Investing in our common stock involves risks. See Risk Factors beginning on page 6.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discount	$	$
Proceeds to Zonagen (before expenses)	$	$

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriter expects to deliver the shares to purchasers on 1 , 2004.

PUNK, ZIEGEL & COMPANY

The date of this prospectus is 1 , 2004.

TABLE OF CONTENTS

You should rely only on the information contained in this prospectus. We have not, and the underwriter has not, authorized anyone to provide you with information that is different. This prospectus is not an offer to sell, nor is it seeking an offer to buy, these securities in any jurisdiction where the offer or sale of these securities is not permitted. You should assume that the information contained in this prospectus is accurate as of the date on the front of this prospectus only. Our business, financial condition, results of operations and prospects may have changed since that date.

Our estimates of market share and market size in this prospectus are based on, in certain cases, public disclosure, industry and trade publications and reports prepared by third parties, which we believe to be reliable but have not been independently verified.

Progenta™, Androxal™ and VASOMAX® are our trademarks. This prospectus also contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.

PROSPECTUS SUMMARY

This summary highlights selected information described more fully elsewhere in this prospectus. This summary does not contain all the information you should consider before investing in our common stock. You should read the entire prospectus, including the financial statements and related notes, before making an investment decision with respect to our common stock. You should pay special attention to the Risk Factors section of this prospectus for a discussion of factors you should consider before investing in our common stock.

References in this prospectus to Zonagen, the company, we, us, our, or similar terms refer to Zonagen, Inc., except as otherwise indicat

Our Business

We are a biopharmaceutical company focused on the development of new drugs to treat hormonal and reproductive system disorders. Our lead product candidate is Progenta, an orally available small molecule compound being developed for the treatment of uterine fibroids and endometriosis. We are developing Progenta under an exclusive, worldwide license from the National Institutes of Health, or NIH. Progenta is being developed to alleviate adverse symptoms associated with both uterine fibroids and endometriosis by selectively blocking the progesterone receptor in women. We believe it may be superior to the current standards of care for the treatment of uterine fibroids and endometriosis, which include surgery and treatment with gonadotropin releasing hormone agonists, or GnRH agonists, such as Lupron®. Unlike Progenta, GnRH agonists induce a low estrogen, menopausal-like state in women, and estrogen is necessary for the maintenance of bone mineral density. Therefore, GnRH agonists tend to promote bone loss and cannot be used for more than six months at a time. When women cease treatment with GnRH agonists, the fibroids rapidly regenerate and symptoms associated with endometriosis quickly reappear. We believe Progenta may provide an attractive alternative to surgery because of its potential to treat these conditions in a long-term, or chronic, fashion, resolving the symptoms that most commonly lead to invasive therapies. We believe Progenta may also be effective as a pre-surgical treatment for uterine fibroids. We currently are conducting a Phase I/ II clinical trial for Progenta in Poland for the treatment of uterine fibroids, which is scheduled to be completed by the end of 2004. We intend to begin a pivotal Phase II/ III trial for Progenta in the United States for the treatment of uterine fibroids during 2005, subject to review of our Phase I/ II data by the U.S. Food and Drug Administration, or FDA.

Our second product candidate is Androxal, an orally available small molecule compound being developed for the treatment of testosterone deficiency in men. Androxal, our proprietary compound, is designed to restore normal testosterone production in males with functional testes and diminished pituitary function, a condition commonly referred to as andropause. We believe that Androxal may be superior to the current gold standard of care, Androgel®, and other similar testosterone replacement therapies for the treatment of men with testosterone deficiency because Androxal avoids the abnormally high peaks in testosterone levels and the elevated levels of dihydrotestosterone, or DHT, which result from use of current testosterone replacement therapies. Both of these effects have been associated with prostate disease and abnormally high peaks of testosterone levels also have been associated with excitation, aggressive behavior, sleeplessness, anxiety, depression and headaches. We recently completed a Phase I/ II clinical trial for Androxal in the United States for the treatment of men with testosterone deficiency and have submitted final data to the FDA in anticipation of a meeting with the FDA scheduled for November 10, 2004 to review our clinical plan for the approval of Androxal and to consider reviewing our pivotal Phase II/ III clinical trials under a special protocol assessment, or SPA.

Progenta

Uterine fibroids are non-cancerous tumors that arise from the smooth muscle layer of the uterus. The National Uterine Fibroid Foundation estimates that possibly as many as 80% of all women in the United States have uterine fibroids, and one in four of these women have symptoms severe enough to require treatment. The primary treatment for uterine fibroids is surgery; drugs are also used to treat uterine fibroids.

The most effective drugs on the market are GnRH agonists, like Lupron, marketed by TAP Pharmaceuticals, which had sales of $787.8 million in the United States and Canada in 2003 for all indications.

We recently completed enrollment of a three-month, 30-patient randomized Phase I/ II clinical trial in Poland comparing Progenta to placebo and Lupron in treating uterine fibroids, and anticipate final data from the trial to be available by early 2005. The preliminary observations from the clinical trial, reported on September 14, 2004, have shown some reduction in fibroid size, as measured by ultrasound, at least numerically equivalent to GnRH agonists. Because this data is still blinded and the effects of a GnRH agonist are best evaluated after at least three months of dosing, these preliminary observations may not be predictive of the final results of this clinical trial or from later stage clinical trials with significantly larger patient populations treated for longer periods of time.

Based upon the final results of our Phase I/II clinical trial for Progenta for the treatment of uterine fibroids, we plan to conduct a Phase II clinical trial in Poland for Progenta for the treatment of endometriosis. Endometriosis occurs when endometrial tissue, which is tissue that normally lines the inside of the uterus, is found outside of the uterus. This misplaced tissue develops into growths or lesions that react to the menstrual cycle the same way that endometrial tissue reacts, which results in internal bleeding and inflammation and can cause pain, infertility, scar tissue formation, adhesions and bowel problems. According to The Endometriosis Association, endometriosis affects 5.5 million women in the United States and Canada and millions more worldwide. We believe Progenta may be superior to current therapies because it is non-invasive, has a positive side effect profile as compared to GnRH agonists, and has the potential for chronic use.

Androxal

Testosterone deficiency in men is linked to several negative physical and mental conditions in the aging male population, including loss of muscle tone, reduced sexual desire, and deterioration of memory and certain other cognitive functions. According to the Urology Channel, recent estimates show that approximately 13 million men in the United States experience testosterone deficiency. Current therapies focus on testosterone replacement by delivering testosterone to the blood stream either through the skin, orally or via injection. The current gold standard in the industry is Androgel, a topical gel marketed by Solvay Pharmaceuticals with sales of approximately $282 million in 2003 in North America.

In July 2004, we released results from a randomized Phase I/ II clinical trial comparing Androxal to placebo and to Androgel in treating men with testosterone deficiency. There were no side effects noted in either the Androxal or Androgel arms of the study that were statistically different than placebo. All three dose levels of Androxal produced statistically significant changes in testosterone from baseline testosterone levels. There were no statistically significant changes within the placebo group. In each patient studied, Androxal produced average testosterone levels that did not exceed the normal range, whereas several Androgel patients had average testosterone levels far above the normal range. We believe these data indicate that the activity and bioavailability of Androxal compare favorably to the current market leader, Androgel. We caution that these results may not be predictive of the results of later stage clinical trials with significantly larger patient populations treated for longer periods of time.

Risks Affecting Us

Our business is subject to numerous risks, as discussed more fully in the section entitled Risk Factors immediately following this prospectus summary. We may not succeed in the clinical development of Progenta or Androxal. Our inability to fulfill our obligations under our licenses with the NIH for Progenta may result in forfeiture of our rights to Progenta. There is a patent holder that claims priority over our patent for Androxal. We cannot assure that we will not have to defend our patents from other infringement claims nor that third parties will not infringe our patents. We will need substantial additional capital to commercialize Progenta and Androxal and such capital may not be available to us when we need it on acceptable terms or at all. We are conducting our clinical trial for Progenta in Poland, and we cannot assure that the FDA will readily accept data from foreign investigators. We may have difficulty in obtaining the compound needed for the manufacture of Progenta in amounts sufficient to continue our clinical trials on a timely basis and at a

reasonable cost. Other companies may produce drugs which are superior to ours or may reach the market before our drugs. We cannot assure that future governmental regulations will not substantially impair our ability to continue without substantial additional costs.

Our Corporate Information

We were formed as a Delaware corporation in 1987 and completed our initial public offering in 1993. Until 2000, we focused our development activities on our phentolamine-based product candidates for the treatment of sexual dysfunction, including VASOMAX. We partnered with Schering-Plough Ltd. and its affiliate to commercialize VASOMAX following completion of our Phase III clinical trials for VASOMAX for the treatment of male erectile dysfunction. After encountering difficulties in obtaining regulatory approval for VASOMAX, we and Schering-Plough terminated our partnership and we attempted to redeploy our assets through a strategic combination from 2000 to 2003. We acquired rights to Progenta from the NIH in 1999 and developed Androxal internally in 2001 but spent limited amounts of cash on preclinical studies for their development during the period when we were considering redeploying our assets. After a Dutch auction self tender offer was completed in January 2004 in which we repurchased 57% of our then-outstanding common stock, we increased our development activities for Progenta and Androxal by commencing a Phase I/ II clinical trial for Progenta in Poland for the treatment of uterine fibroids and completing our Phase I/ II clinical trial for Androxal in the United States for the treatment of men with testosterone deficiency.

Our principal executive offices are located at 2408 Timberloch Dr., Suite B-1, The Woodlands, Texas 77380, and our telephone number is (281) 719-3400. Our website address is *http://www.zonagen.com.* We do not incorporate the information on, or accessible through, our website into this prospectus, and you should not consider it part of this prospectus.

The Offering

Common stock offered by us	4,000,000 shares
Common stock to be outstanding immediately after this offering	8,992,901 shares
Use of proceeds	We estimate that our net proceeds from this offering will be approximately $ l million. We plan to use the proceeds to continue clinical development of our Progenta and Androxal product candidates. In addition, we may use a portion of the net proceeds for working capital and general corporate purposes. Pending these uses, the net proceeds will be invested in investment-grade, interest-bearing securities.
Nasdaq SmallCap ticker symbol	ZONA
Pacific Stock Exchange ticker symbol	ZNG

The number of shares of common stock outstanding immediately after this offering is based on 4,992,901 shares outstanding as of October 19, 2004 and excludes:

- 1,786,846 shares of our common stock issuable upon exercise of options previously granted to employees and non-employee directors;
- 381,933 additional shares of our common stock that are available for grant and reserved for issuance under our 2004 stock option plan and our 2000 director plan; and
- 127,366 shares reserved for issuance under our 2000 employee stock purchase plan.

Unless otherwise indicated, the information in this prospectus assumes that the underwriter will not exercise its over-allotment option.

Summary Consolidated Financial Information

The summary consolidated financial information for the years ended December 31, 2001, 2002 and 2003 were derived from, and are qualified by reference to, our consolidated financial statements, including the notes thereto, contained elsewhere in this prospectus. The unaudited consolidated summary financial information for the nine months ended September 30, 2003 and September 30, 2004 and the unaudited consolidated balance sheet data at September 30, 2004 were derived from, and are qualified by reference to, our unaudited consolidated financial statements included elsewhere in this prospectus. The following data should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations contained herein.

	For the Year Ended December 31,			Nine Months Ended September 30,	
	2001	2002	2003	2003	2004
					(Unaudited)
	(In thousands except per share amounts)				
Revenues and other income					
Licensing fees	$ 2,162	$ 4,228			
Products royalties	58				
Research and development grants	115	315	$ 595	$ 459	$ 118
Interest income	1,526	711	318	254	75
Gain on disposal of fixed assets			102	102	
Other income					35
Total revenues and other income	3,861	5,254	1,015	815	228
Expenses					
Research and development	3,028	6,420	2,161	1,583	1,914
General and administrative	1,672	2,716	2,183	1,707	1,268
Interest expense and amortization of intangibles					
Total expenses	4,700	9,136	4,344	3,290	3,182
Loss from continuing operations	(839)	(3,882)	(3,329)	(2,475)	(2,954)
Loss from discontinued operations					
Gain on disposal					
Net loss before cumulative effect of change in accounting principle	(839)	(3,882)	(3,329)	(2,475)	(2,954)
Cumulative effect of change in accounting principle					
Net loss	$ (839)	$ (3,882)	$ (3,329)	$ (2,475)	$ (2,954)
Loss per share basic and diluted	$ (0.07)	$ (0.34)	$ (0.29)	$ (0.22)	$ (0.57)
Shares used in income (loss) per share calculation:					
Basic	11,333	11,412	11,487	11,489	5,159
Diluted	11,333	11,412	11,487	11,489	5,159

	As of September 30, 2004	
	Actual	As Adjusted (1)
	(Unaudited) (In thousands)	
Balance sheet data:		
Cash and cash equivalents	$2,556	$
Marketable securities	4,000	
Total assets	7,046	
Total current liabilities	415	
Total stockholders equity	6,631	

(1) The as adjusted balance sheet data as of September 30, 2004 gives effect to the receipt of net proceeds of $ l million from the sale of 4,000,000 shares of common stock offered by this prospectus, after deducting the underwriter s discount and estimated offering expenses payable by us.

RISK FACTORS

In considering whether to invest in our common stock, you should carefully read and consider the risks described below, together with all of the information we have included in this prospectus.

Risks Relating to Our Business

Our product candidates are at an early stage of development, and if we are not able to successfully develop and commercialize them, we may not generate sufficient revenues to continue our business operations.

We currently have only two product candidates, and both are in early stages of development. We recently completed a Phase I/ II clinical trial for Androxal in the United States for the treatment of men with testosterone deficiency, and Progenta is currently undergoing a Phase I/ II clinical trial in Poland for the treatment of uterine fibroids. We have expended significant time, money and effort in the development of Progenta and Androxal and we will have to spend considerable additional time, money and effort before seeking regulatory approval to market these product candidates.

Our business depends primarily on our ability to successfully complete clinical trials, obtain required regulatory approvals and successfully commercialize Progenta and Androxal. If we fail to commercialize Progenta and Androxal, we may be unable to generate sufficient revenues to attain profitability or continue our business operations and our reputation in the industry and in the investment community could likely be significantly damaged, each of which would cause our stock price to decline.

We licensed our rights to Progenta from the National Institutes of Health, or NIH, and our inability to fulfill our commitments and obligations under such license may result in forfeiture of our rights.

Our rights to Progenta are licensed exclusively to us from the NIH under a license agreement. This license agreement contains numerous detailed performance obligations, with time sensitive dates for compliance, relating to clinical development and commercialization activities required by us or our designated third-party providers, as well as additional financial milestones and royalties. Failure to achieve the benchmarks specified in the commercial development plan attached to the license agreement could result in termination of the license agreement and the loss of our rights to develop and commercialize Progenta. During the period when we were considering redeployment of our assets, we were not in compliance with all of the original requirements stated in the commercial development plan. In July 2002, the license agreement was amended to include a revision of the original commercial development plan relating to the targeted dates for certain objectives. Additional updates of the original commercial development plan have been reached with the NIH thereafter in order to expedite development. There can be no assurance that we will be able to meet any or all of such performance objectives in the future on a timely basis or at all, or that, if we fail to meet any of such objectives, the NIH will again agree to amend such agreement to our satisfaction. Should the NIH terminate the license agreement, we would lose all rights to commercialize Progenta, which would have a material adverse effect on us.

There is a patent holder that claims priority over our patent for Androxal.

U.S. Patent No. 6,391,920 was issued to a competitor on May 21, 2002 and is directed to a method of treating testosterone deficiency in men using an anti-estrogen such as clomiphene. Clomiphene has traditionally been used to treat testosterone deficiency. Androxal is a purified form of this compound. This patent could block our rights to use Androxal for the intended use; however, on March 9, 2004, the PTO issued an order granting our request for ex parte reexamination of this patent based on prior printed publications. Pursuant to this reexamination, the PTO subsequently issued a non-final office action rejecting all of the patent claims in this competing patent. The other party has until November 9, 2004 to respond to the office action. If they can do so successfully and if the PTO upholds their patent, we may then be required to license rights to the patent from the other party if we want to continue the development of Androxal. Such license may not be available on acceptable terms, or at all. If this were to occur, we would not be able to develop or commercialize Androxal.

If we fail to obtain the capital necessary to fund our operations, we will have to delay, reduce or eliminate our research and development programs or commercialization efforts.

We expect to make additional capital outlays and to increase operating expenditures over the next several years to support our preclinical development and clinical trial activities. Our existing financial resources, together with the expected proceeds of this offering, are expected to be sufficient to fund our operations through the end of 2005. Therefore we will need to seek additional funding through public or private financings, including equity financings, and through other means, including collaborations and license agreements. We do not know whether additional financing will be available when needed, or that, if available, we will obtain financing on terms favorable to our stockholders or us. If adequate funds are not available to us, we may be required to:

delay, reduce the scope of or eliminate one or more of our development programs;

liquidate and dissolve our company;

seek collaborators for our product candidates at an earlier stage than otherwise would be desirable and on terms that are less favorable than might otherwise be available; or

relinquish, license or otherwise dispose of rights to technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves on terms that are less favorable than might otherwise be available.

Our future capital requirements will depend upon a number of factors, including:

the size, complexity, results and timing of our clinical programs;

the cost to obtain sufficient supply of the compounds necessary for our product candidates at a reasonable cost;

the time and costs involved in obtaining regulatory approvals;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims; and

competing technological and market developments.

These factors could result in variations from our currently projected operating and liquidity requirements.

We have a history of operating losses, and we expect to incur increasing net losses and may not achieve or maintain profitability for some time or at all.

We have experienced significant operating losses in each fiscal year since our inception. As of September 30, 2004, we had an accumulated deficit of approximately $86.0 million. We expect to continue incurring net losses and may not achieve or maintain profitability for some time or at all. As we increase expenditures for clinical development of Progenta and Androxal, we expect our operating losses to increase for at least the next few years. Our ability to achieve profitability will depend, among other things, on successfully completing the development of Progenta and Androxal, obtaining regulatory approvals, establishing marketing, sales and manufacturing capabilities or collaborative arrangements with others that possess such capabilities, and raising sufficient funds to finance our activities. There can be no assurance that we will be able to achieve profitability or that profitability, if achieved, can be sustained.

Raising additional funds by issuing securities or through collaboration and licensing arrangements may cause dilution to existing stockholders, restrict our operations or require us to relinquish proprietary rights.

We may raise additional funds through public or private equity offerings, debt financings or corporate collaborations and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional capital by issuing equity securities, our stockholders ownership will be diluted. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem capital

stocks or make investments. In addition, if we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. For example, we might be forced to relinquish all or a portion of our sales and marketing rights with respect to Progenta, Androxal or other potential products or license intellectual property that enables licensees to develop competing products.

Because the data from preclinical studies and early clinical trials for Progenta and Androxal are not necessarily predictive of future results, we can provide no assurances that these product candidates will have favorable results in clinical trials or receive regulatory approval.

Before we can obtain regulatory approval for the commercial sale of any product candidate that we wish to develop, we are required to complete preclinical development and extensive clinical trials in humans to demonstrate its safety and efficacy. Positive data from preclinical studies or early clinical trials should not be relied upon as evidence that those studies or trials will produce positive results, or that later or larger-scale clinical trials will succeed. Initial clinical trials for Progenta and Androxal have been conducted only in small numbers of patients that may not fully represent the diversity present in larger populations, and thus the limited data we have obtained may not predict results from studies in larger numbers of patients drawn from more diverse populations, and therefore may not predict the ability of Progenta to treat uterine fibroids and endometriosis or Androxal to treat testosterone deficiency. We will be required to demonstrate through larger-scale clinical trials that these product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. There is typically an extremely high rate of attrition from the failure of drug candidates proceeding through clinical trials. If Progenta, Androxal, or any other potential future product candidate fails to demonstrate sufficient safety and efficacy in any clinical trial, we would experience potentially significant delays in, or be required to abandon, development of that product candidate. If we delay or abandon our development efforts related to Progenta or Androxal, we may not be able to generate sufficient revenues to continue operations or become profitable.

We have not filed an Investigational New Drug application to conduct clinical trials for Progenta in the United States and we may not be able to obtain FDA approval of such application to permit us to conduct clinical trials for Progenta in the United States.

We are currently conducting our Phase I/ II clinical trial for Progenta for the treatment of uterine fibroids in Poland. Prior to commencing any clinical trials for Progenta in the United States, we will need to submit an Investigational New Drug, or IND, application to the FDA. Any IND application that we submit to the FDA for Progenta will likely incorporate the results of our clinical trial in Poland. The FDA may not accept the results of this clinical trial and may request further preclinical data before approving the IND. Moreover, the FDA may subject the trial data that we submit to additional scrutiny and we may incur additional costs and delays responding to FDA requests for supplemental information or clarification. If we are unable to obtain FDA approval for an IND for Progenta, we will not be permitted to conduct clinical trials for Progenta in the United States and ultimately seek or obtain regulatory approval for commercialization in the United States. As a result, any delay in an IND becoming effective for Progenta would delay the further development and potential commercialization of our lead product candidate and delay our ability to generate product sales.

Delays in the commencement of clinical testing of our current and potential product candidates could result in increased costs to us and delay our ability to generate revenues.

Our product candidates will require continued preclinical testing and extensive clinical trials prior to the submission of a regulatory application for commercial sales. We recently completed our Phase I/ II clinical trial for Androxal in the United States for the treatment of men with testosterone deficiency and are continuing our Phase I/ II clinical trail for Progenta in Poland and, as a result, have very limited experience conducting clinical trials. In part, because of this limited experience, we do not know whether future planned clinical trials will begin on time, if at all. Delays in the commencement of clinical testing could significantly increase our product development costs and delay any product commercialization. In addition, many of the

factors that may cause, or lead to, a delay in the commencement of clinical trials may also ultimately lead to denial of regulatory approval of a product candidate.

The commencement of clinical trials can be delayed for a variety of reasons, including delays in:

demonstrating sufficient safety and efficacy in past clinical trials to obtain regulatory approval to commence a further clinical trial;

reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites;

manufacturing sufficient quantities of a product candidate;

obtaining approval of an IND application from the FDA for Progenta and any other potential product candidates; and

obtaining institutional review board approval to conduct a clinical trial at a prospective site.

In addition, the commencement of clinical trials may be delayed due to insufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial.

Delays in the completion of, or the termination of, clinical testing of our current and potential product candidates could result in increased costs to us, and could delay or prevent us from generating revenues.

Once a clinical trial has begun, it may be delayed, suspended or terminated by us or the FDA, or other regulatory authorities due to a number of factors, including:

ongoing discussions with the FDA or other regulatory authorities regarding the scope or design of our clinical trials;

failure to conduct clinical trials in accordance with regulatory requirements;

lower than anticipated retention rate of patients in clinical trials;

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

lack of adequate funding to continue clinical trials;

negative results of clinical trials;

requests by the FDA for supplemental information on, or clarification of, the results of our clinical trials in Poland;

insufficient supply or deficient quality of drug candidates or other materials necessary for the conduct of our clinical trials; or

serious adverse events or other undesirable drug-related side effects experienced by participants.

Many of these factors that may lead to a delay, suspension or termination of clinical testing of a current or potential product candidate may also ultimately lead to denial of regulatory approval of a current or potential product candidate. We experienced a clinical hold beginning in 1999 during our development of VASOMAX and were forced to abandon development of that product candidate. If we experience delays in the completion of, or termination of, clinical testing of any product candidates in the future, our financial results and the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed.

Even if we successfully complete clinical trials for Progenta and Androxal, there are no assurances that we will be able to submit, or obtain FDA approval of, a new drug application.

There can be no assurance that, if our clinical trials for Progenta and Androxal are successfully completed, we will be able to submit a new drug application, or NDA, to the FDA or that any NDA we submit will be approved by the FDA in a timely manner, if at all. If we are unable to submit a NDA with respect to Progenta or Androxal, or if any NDA we submit is not approved by the FDA, we will be unable to commercialize that product. The FDA can and does reject NDAs and requires additional clinical trials, even when drug candidates perform well or achieve favorable results in large-scale Phase III clinical trials. If we fail to commercialize Progenta or Androxal, we may be unable to generate sufficient revenues to continue operations or attain profitability and our reputation in the industry and in the investment community would likely be damaged, each of which would cause our stock price to significantly decrease.

If commercialized, our product candidates may not be approved for sufficient governmental or third-party reimbursements, which would adversely affect our ability to market our product candidates.

In the United States and elsewhere, sales of pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from third-party payers, such as government and private insurance plans. Since we have no commercial products, we have not had to face this issue yet, however, third-party payers are increasingly challenging the prices charged for medical products and services. It will be time consuming and expensive for us to go through the process of seeking reimbursement from Medicaid, Medicare and private payers for Progenta and Androxal. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis. The passage of the Medicare Prescription Drug and Modernization Act of 2003 imposes new requirements for the distribution and pricing of prescription drugs which may negatively affect the marketing of our potential products.

Our plan to use collaborations to leverage our capabilities may not be successful.

As part of our business strategy, we intend to enter into collaboration arrangements with strategic partners to develop product candidates. For our collaboration efforts to be successful, we must identify partners whose competencies complement ours. We must also successfully enter into collaboration agreements with them on terms attractive to us and integrate and coordinate their resources and capabilities with our own. We may be unsuccessful in entering into collaboration agreements with acceptable partners or negotiating favorable terms in these agreements. Also, we may be unsuccessful in integrating the resources or capabilities of these collaborators. In addition, our collaborators may prove difficult to work with or less skilled than we originally expected. If we are unsuccessful in our collaborative efforts, our ability to develop and market product candidates could be severely limited.

If we successfully develop products but those products do not achieve and maintain market acceptance, our business will not be profitable.

Even if Progenta and Androxal are approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product by physicians, healthcare professionals and third-party payers and our profitability and growth will depend on a number of factors, including:

- our ability to provide acceptable evidence of safety and efficacy;
- relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- availability, effectiveness and cost of alternative treatments;
- pricing and cost effectiveness;

effectiveness of our or our collaborators sales and marketing strategy; and

our ability to obtain sufficient third-party insurance coverage or reimbursement.

If Progenta does not provide a treatment regimen that is more beneficial than Lupron, a GnRH agonist and the current standard of care, or otherwise provide patient benefit, it likely will not be accepted favorably by the market. Similarly, if Androxal does not provide a treatment regime that is more beneficial than Androgel, the current standard of care for the treatment of testosterone deficiency, or otherwise provide patient benefit, it likely will not be accepted favorably by the market. If any products we may develop do not achieve market acceptance, then we will not generate sufficient revenue to achieve or maintain profitability.

In addition, even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if:

new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete;

unforeseen complications arise with respect to use of our products; or

sufficient third-party insurance coverage or reimbursement does not remain available.

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

Currently, we do not have the ability internally to manufacture the product candidates that we need to conduct our clinical trials. We have entered into purchase orders with third-party manufacturers to produce our supplies of Progenta and Androxal; however, we have no long term contracts with suppliers of either product candidate.

For the foreseeable future, we expect to continue to rely on third-party manufacturers and other third parties to produce, package and store sufficient quantities of Progenta, Androxal and any future product candidates for use in our clinical trials. If our third-party manufacturers fail to deliver our product candidates 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 or otherwise discontinue development and production of our product candidates. We may also be required to enter into long-term manufacturing agreements that contain exclusivity provisions and/or substantial termination penalties. In addition, third-party manufacturers may 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.

We also depend on outside vendors for the supply of raw materials used to produce our product candidates. If third-party suppliers were to cease production or otherwise fail to supply us with quality raw materials and we were 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.

Our product candidates have only been manufactured in small quantities to date, and we may face delays or complications in manufacturing quantities of our product candidates in sufficient quantities to meet the demands of late stage clinical trials and marketing.

We cannot assure that we will be able to successfully increase the manufacturing capacity or scale-up manufacturing volume per batch, whether on our own or in reliance on third-party manufacturers, for any of our product candidates in a timely or economical manner, or at all. To date our product candidates have been manufactured exclusively by third parties in small quantities for pre-clinical and clinical trials. We will need to arrange for the production of significantly larger quantities of our product candidates for future clinical

trials and for future commercial sale in the event that our product candidates are approved by the FDA or foreign regulatory bodies. Significant scale-up of manufacturing may require certain additional validation studies, which the FDA must review and approve. If we or our third-party manufacturers are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply of that product candidate.

Our product candidates require precise, high-quality manufacturing which may not be available at acceptable costs.

Progenta is a novel compound that has never been produced in large scale. As in the development of any new compound, there are underlying risks associated with its manufacture. These risks include, but are not limited to, cost, process scale-up, process reproducibility, construction of a suitable process plant, timely availability of raw materials, as well as regulatory issues associated with the manufacture of an active pharmaceutical agent. Any of these risks may prevent us from successfully developing Progenta. Our failure, or the failure of our third-party manufacturers to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors and reliable product packaging for diverse environmental conditions, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

We may experience delays in the development of our product candidates if the third-party manufacturers of our product candidates cannot meet FDA requirements relating to Good Manufacturing Practices.

Our third-party manufacturers are required to produce our product candidates under FDA current Good Manufacturing Practices in order to meet acceptable standards for our clinical trials. If such standards change, the ability of third-party manufacturers to produce our product candidates on the schedule we require for our clinical trials may be affected. In addition, third-party manufacturers may not perform their obligations under their agreements with us or may discontinue their business before the time required by us to gain approval for or commercialize our product candidates. Any difficulties or delays in the manufacturing and supply of our product candidates could increase our costs or cause us to lose revenue or postpone or cancel clinical trials.

The FDA also requires that we demonstrate structural and functional comparability between the same drug product produced by different third-party manufacturers. Because we may use multiple sources to manufacture Progenta and Androxal, we may need to conduct comparability studies to assess whether manufacturing changes have affected the product safety, identity, purity or potency of any commercial product candidate compared to the product candidate used in clinical trials. If we are unable to demonstrate comparability, the FDA could require us to conduct additional clinical trials, which would be expensive and significantly delay commercialization of our product candidates.

We rely on third parties to conduct clinical trials for our product candidates, and their failure to timely and properly perform their obligations may result in costs and delays that prevent us from obtaining regulatory approval or successfully commercializing our product candidates.

We rely on outside scientific collaborators, such as researchers at clinical research organizations and universities, in certain areas that are particularly relevant to our research and product development plans, such as the conduct of clinical trials. The competition for these relationships is intense, and we may not be able to maintain our relationships with them on acceptable terms. These outside collaborators generally may terminate their engagements with us at any time. As a result, we can control their activities only within certain limits, and they will devote only a certain amount of their time conducting research on and trials of our product candidates and assisting in developing them. If they do not successfully carry out their duties under their agreements with us, fail to inform us if these trials fail to comply with clinical trial protocols, or fail to meet expected deadlines, our clinical trials may need to be extended, delayed or terminated. We may not be able to enter into replacement arrangements without undue delays or excessive expenditures. If there are delays in testing or regulatory approvals as a result of the failure to perform by our scientific collaborators

or other outside parties, our drug development costs will increase and we may not be able to attain regulatory approval for or successfully commercialize our product candidates.

We face substantial uncertainty in our ability to protect our patents and proprietary technology.

Our ability to commercialize our products will depend, in part, on our or our licensors ability to obtain patents, to enforce those patents and preserve trade secrets, and to operate without infringing on the proprietary rights of others. The patent positions of biopharmaceutical companies are highly uncertain and involve complex legal and factual questions. There can be no assurance that:

patent applications owned by or licensed to us will result in issued patents;

patent protection will be secured for any particular technology;

any patents that have been or may be issued to us or our licensors will be valid or enforceable;

any patents will provide meaningful protection to us;

others will not be able to design around the patents; or

our patents will provide a competitive advantage or have commercial application.

The failure to obtain and maintain adequate patent protection would have a material adverse effect on us and may adversely affect our ability to enter into, or affect the terms of, any arrangement for the marketing of any product.

We cannot assure that our patents will not be challenged by others.

There can be no assurance that patents owned by or licensed to us will not be challenged by others. We could incur substantial costs in proceedings, including interference proceedings before the U.S. Patent and Trademark Office, or PTO, and comparable proceedings before similar agencies in other countries in connection with any claims that may arise in the future. These proceedings could result in adverse decisions about the patentability of our or our licensors inventions and products, as well as about the enforceability, validity or scope of protection afforded by the patents. Any adverse decisions about the patentability of our product candidates could cause us to either lose rights to develop and commercialize our product candidates or to license such rights at substantial cost to us. In addition, even if we were successful in such proceedings, the cost and delay of such proceedings would most likely have a material adverse effect on our business.

We cannot assure that our manufacture, use or sale of Progenta and Androxal will not infringe on the patent rights of others.

There can be no assurance that the manufacture, use or sale of Progenta or Androxal and any potential future product candidates will not infringe the patent rights of others. We may be unable to avoid infringement of the patent rights of others and may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. There can be no assurance that a license will be available to us on terms and conditions acceptable to us, if at all, or that we will prevail in any patent litigation. Patent litigation is extremely costly and time-consuming, and there can be no assurance that we will have sufficient resources to defend any possible litigation related to such infringement. If we do not obtain a license on acceptable terms under such patents, or are found liable for infringement, or are not able to have such patents declared invalid, we may be liable for significant money damages, may encounter significant delays in bringing Progenta and Androxal to market, or may be precluded from participating in the manufacture, use or sale of Progenta or Androxal, any of which would materially and adversely effect our business.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information and may not adequately protect our intellectual property, nor will such agreements prevent third parties from independently discovering technology similar to or in competition with our intellectual property.

We rely on trade secrets and other unpatented proprietary information in our product development activities. To the extent we rely on trade secrets and unpatented know-how to maintain our competitive technological position, there can be no assurance that others may not independently develop the same or similar technologies. We seek to protect trade secrets and proprietary knowledge, in part, through confidentiality agreements with our employees, consultants, advisors, collaborators and contractors. Nevertheless, these agreements may not effectively prevent disclosure of our confidential information and may not provide us with an adequate remedy in the event of unauthorized disclosure of such information. If our employees, scientific consultants or collaborators develop inventions or processes independently that may be applicable to our technologies, product candidates or products, disputes may arise about ownership of proprietary rights to those inventions and processes. Such inventions and processes will not necessarily become our property, but may remain the property of those persons or their employers. Protracted and costly litigation could be necessary to enforce and determine the scope of our proprietary rights. If we fail to obtain or maintain trade secret protection for any reason, the competition we face could increase, reducing our potential revenues and adversely affecting our ability to attain or maintain profitability.

Our liability insurance may not provide adequate coverage nor may it always be available on favorable terms or at all.

Neither Progenta nor Androxal has been approved for commercial sale. However, the current and future use of our product candidates by us and potential 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, potential 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 losses. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or for liabilities in excess of our insurance limits, our assets may not be sufficient to cover such claims and our business operations could be impaired.

We face significant competition with many companies with substantially greater resources than we have and other possible advantages.

We are engaged in biopharmaceutical product development, an industry that is characterized by extensive research efforts and rapid technological progress. The biopharmaceutical industry is also highly competitive. Our success will depend on our ability to acquire, develop and commercialize products and our ability to establish and maintain markets for Androxal and Progenta or any products for which we receive marketing approval. Potential competitors in North America, Europe and elsewhere include major pharmaceutical companies, specialty pharmaceutical companies and biotechnology firms, universities and other research institutions and government agencies. Many of our competitors have substantially greater research and development and regulatory capabilities and experience, and substantially greater management, manufacturing, distribution, marketing and financial resources, than we do. Accordingly, our competitors may:

develop or license products or other novel technologies that are more effective, safer or less costly than the product candidates that we are developing;

obtain regulatory approval for products before we do; or

have the ability to commit more resources than we can to developing, marketing and selling competing products.

The main therapeutic products competitive with Progenta for the treatment of uterine fibroids and endometriosis are GnRH agonists, especially Lupron, which is marketed by TAP Pharmaceuticals. There are additional companies developing similar progesterone-blocking technology. Asoprisnil, an anti-progestin being developed by TAP Pharmaceuticals in partnership with Schering AG, is currently in Phase III clinical trials. TAP Pharmaceuticals is a much larger company than we are with greater resources and greater ability to promote their products than we currently have. In addition, surgical treatment of both uterine fibroids and endometriosis competes with Progenta by removing uterine fibroids and by removing misplaced tissue in women with endometriosis.

Our main competitors for the treatment of testosterone deficiency are the testosterone replacement therapies currently being marketed. The current gold standard of care is Androgel, a topical gel for the replacement of testosterone developed by Solvay Pharmaceuticals. Solvay is a much larger company than we are with greater resources and marketing ability. Androxal would also compete with other forms of testosterone replacement therapies such as oral treatments, patches, injectables and a tablet applied to the upper gum. There is another topical gel currently marketed by Auxilium Pharmaceuticals called Testim®, and a transdermal patch marketed by Watson Pharmaceuticals called AndroDerm®. Although we believe we compete favorably against these products, there can be no assurance at this point that our product candidates will be more successful than competitive products. In addition, other potential competitors may be developing testosterone therapies similar to ours.

We are thinly staffed and highly dependent on a limited number of management persons and key personnel, and if we lose these members of our team or are unable to attract and retain additional qualified personnel, our future growth and ability to compete would suffer.

The competition for qualified personnel in the biopharmaceutical field is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical and managerial employees. We have only four full-time employees at the present time, including our President and CEO, Joseph S. Podolski, and our Vice President, Business Development and CFO, Louis Ploth, Jr. We are highly dependent on Messrs. Podolski and Ploth for the management of our company and the development of our technologies. Both Messrs. Podolski and Ploth have employment agreements with us. There can be no assurance that either or both of Messrs. Podolski and Ploth will remain with us through development of our current product candidates. We do not maintain key person life insurance on any of our directors, officers or employees. The loss of the services of Mr. Podolski or Mr. Ploth could delay or curtail our research and product development efforts.

Additionally, in order to commercialize our products successfully, we will be required to expand our workforce, particularly in the areas of manufacturing, clinical trials management, regulatory affairs, business development, sales and marketing and administrative and accounting functions. These activities will require the addition of new personnel and the development of additional expertise by management. We face intense competition for qualified individuals from numerous biopharmaceutical companies, as well as academic and other research institutions. To the extent we are not able to attract and retain employees on favorable terms, we may face delays in the development or commercialization of our product candidates and extensive costs in retaining current employees or searching for and training new employees.

Healthcare reform measures could adversely affect our business.

The business and financial condition of pharmaceutical companies are affected by the efforts of governmental and third-party payers to contain or reduce the costs of healthcare. In the United States and in foreign jurisdictions there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the healthcare system. For example, in some countries other than the United States, pricing of prescription drugs is subject to government control, and we expect proposals to implement similar controls in the United States to continue. The pendency or approval of such proposals could result in a decrease in our stock price or limit our ability to raise capital or to obtain strategic collaborations or licenses.

Risks Relating to this Offering

Our stock price is, and we expect it to remain, volatile, which could limit investors ability to sell stock at a profit.

The volatile price of our common stock makes it difficult for investors to predict the value of their investment, to sell shares at a profit at any given time, or to plan purchases and sales in advance. For example, for the period beginning on the first trading day following completion of our self tender offer (January 8, 2004) and ending on October 19, 2004 (as reported on the Nasdaq National Market through July 7, 2004 and subsequently on the Nasdaq SmallCap Market), a share of our common stock traded at prices ranging between $1.84 to $5.95. A variety of factors may affect the market price of our common stock. These include, but are not limited to:

publicity regarding actual or expected clinical trial results relating to products under development by our competitors or us;

delay or failure in initiating, completing or analyzing preclinical or clinical trials or unsatisfactory design or result of these trials;

achievement or rejection of regulatory approvals by our competitors or us;

announcements of technological innovations or new commercial products by our competitors or us;

developments concerning proprietary rights, including patents;

developments concerning our license agreement with the NIH and other current or potential collaborations;

regulatory developments in the United States and foreign countries;

economic or other crises and other external factors;

period-to-period fluctuations in our revenue and other results of operations;

changes in financial estimates by securities analysts and our ability to meet or exceed such estimates; and

actual or anticipated sales of debt or equity securities by us.

We will not be able to control many of these factors, and we believe that period-to-period comparisons of our financial results will not necessarily be indicative of our future performance. If our revenues, if any, in any particular period do not meet expectations, we may not be able to adjust our expenditures in that period, which could cause our operating results to suffer further. If our operating results in any future period fail to meet or exceed the expectations of securities analysts or investors, our stock price may decline by a significant amount.

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

We expect to sell additional equity securities, which would cause dilution.

We expect to sell more equity securities in the future to obtain operating funds. We may sell these securities at a discount to the market price. Any future sales of equity will dilute the holdings of existing stockholders, possibly reducing the value of their investment.

Recent trading in our common stock has been limited, so investors may not be able to sell significant amounts of our common stock at prevailing prices.

Since the first trading day after completion of our tender offer on January 8, 2004 through September 30, 2004, the average daily trading volume in our common stock was approximately 40,400 shares. In the last 30 days, the average daily trading volume in our common stock was approximately 7,500 shares. Although trading volume in our common stock may increase after this offering, it may be difficult for investors to sell their shares in the public market at any given time at prevailing prices.

Investors in this offering will suffer immediate dilution.

As of September 30, 2004 we had a net tangible book value of approximately $6.3 million, or approximately $1.25 per share of common stock, assuming no exercise of any options. The net tangible book value per share is substantially less than the current market price per share. If investors in this offering pay more than the net tangible book value per share for stock in this offering, they will suffer immediate dilution.

As of September 30, 2004, holders of our outstanding options have the right to acquire 1,836,846 shares issuable on the exercise of stock options, at exercise prices ranging from $1.70 to $33.25 per share. If the holders convert or exercise those stock options, investors in this offering may experience additional dilution in the net tangible book value of our common stock they purchase. In addition, the sale or availability for sale of the underlying shares in the market could depress our stock price. We have registered all of the underlying shares listed above. Holders of registered underlying shares could resell the shares immediately upon issuance, resulting in significant downward pressure on our stock price.

Anti-takeover provisions could make it more difficult for a third party to acquire us.

Our board of directors has the authority to issue up to 5,000,000 shares of preferred stock and to determine the price, rights, preferences, privileges and restrictions, including voting rights, of those shares without any further vote or action by our stockholders. The rights of holders of our common stock may be subject to, and may be adversely affected by, the rights of the holders of any preferred stock that may be issued in the future. The issuance of preferred stock may have the effect of delaying, deferring or preventing a change of control without further action by the stockholders and may adversely affect the voting and other rights of the holders of common stock.

In addition, we have a stockholder Rights Agreement currently in effect until September 2005 which could have the effect of deterring, delaying or preventing a change of control without further action by our board of directors.

Finally, state anti-takeover laws in Delaware related to corporate takeovers may deter, prevent or delay a change of control.

Our management will have broad discretion in allocating the net proceeds from this offering, and the failure of our management to apply the net proceeds from this offering effectively could harm our business.

We currently intend to use the net proceeds from the sale of the common stock offered hereby for continued clinical development of our Progenta and Androxal product candidates. In addition, we may use a portion of the net proceeds for working capital and general corporate purposes. We have not determined the amount of net proceeds from the sale of our common stock pursuant to this offering that we will use for each of these purposes. Accordingly, our management will retain broad discretion as to the allocation of the net proceeds of this offering. The failure of management to apply these funds effectively could negatively impact our business.

Our common stock could be delisted from the Nasdaq SmallCap Market, which would adversely affect the liquidity of our common stock.

The Nasdaq Stock Market has established rules and policies with respect to the continued listing of securities on the Nasdaq SmallCap Market. In executing these policies, the Nasdaq Stock Market has

established standards and identified events following which it will normally consider suspending dealings in or removing a security from listing (delisting) on the Nasdaq SmallCap Market. We were recently required to move to the Nasdaq SmallCap Market because we no longer met the Nasdaq National Market requirement of maintaining stockholders equity of at least $10 million. The Nasdaq SmallCap Market has a requirement that an issuer have at least $2.5 million in stockholders equity for continued listing, among other requirements. If we are able to complete the offering contemplated hereby, we believe that we will continue to meet this listing requirement until the end of 2005; however, we cannot assure that we will be able to do so given the uncertainties of our capital requirements in developing our technologies.

The Nasdaq SmallCap Market also has a minimum bid price per share requirement for listed securities of $1.00. It is possible that our price per share could fall below this minimum amount any time before or following completion of the offering. If we are forced to delist our common stock and we do not qualify for listing on another exchange or in a consolidated quotation system, our common stock might continue to be traded as an unlisted company in an over-the-counter market, such as the Over-the-Counter Bulletin Board or the pink sheets. There can be no assurance of any trading activity or the level of liquidity or market price of our common stock should it be delisted from the Nasdaq SmallCap Market.

If our common stock were delisted from the Nasdaq SmallCap Market, our common stock would be subject to the penny stock rules, which would adversely affect the liquidity of our common stock.

If Nasdaq delisted our common stock, it could become subject to Rule 15g-9 under the Securities Exchange Act of 1934, as amended, or Exchange Act, which imposes additional sales practice requirements on broker-dealers that sell such securities to persons other than established customers and accredited investors (generally, individuals with net worth in excess of $1,000,000 or annual incomes exceeding $200,000, or $300,000 together with their spouses). For transactions covered by this rule, a broker-dealer must make a special suitability determination for the purchaser and receive the purchaser s written consent to the transaction prior to sale. Consequently, this rule may adversely affect the ability of the holders of our common stock to sell their shares in the secondary market.

SEC regulations define a penny stock to be any non-Nasdaq equity security that has a market price (as therein defined) of less than $5.00 per share or with an exercise price of less than $5.00 per share, subject to certain exceptions). For any transaction involving a penny stock, unless exempt, the rules require delivery, prior to any transaction in a penny stock, of a disclosure schedule prepared by the SEC relating to the penny stock market. The SEC also requires disclosure about commissions payable to both the broker-dealer and the registered representative and current quotations for the securities. Finally, the SEC requires monthly statements to be sent disclosing recent price information for the penny stock held in the account and information on the limited market in penny stocks.

These penny stock restrictions will not apply to our common stock if it remains listed on Nasdaq and meets certain price and volume requirements on a current and continuing basis or meets certain minimum net tangible assets or average revenue criteria. We cannot ensure that our common stock will qualify for exemption from these restrictions. Even if our common stock were exempt from such restrictions, we would remain subject to Section 15(b)(6) of the Exchange Act, which gives the SEC the authority to prohibit any person engaged in unlawful conduct while participating in a distribution of a penny stock from associating with a broker-dealer or participating in a distribution of a penny stock, if the SEC finds that such a restriction would be in the public interest. If our common stock were subject to the rules on penny stocks, the market liquidity for our common stock could be severely and adversely affected.

Our former independent public accountant, Arthur Andersen LLP, has ceased operations and investors may be unable to exercise effective remedies against it in any legal action.

Arthur Andersen LLP was our independent auditor for the eight years ended December 31, 2001. On June 15, 2002, a jury in Houston, Texas found Arthur Andersen LLP guilty of federal obstruction of justice charges arising from the federal government s investigation of Enron Corp. On June 15, 2002, Arthur Andersen LLP ceased practicing before the SEC and substantially all of its personnel have left the firm,

including the individuals responsible for auditing our audited financial statements for the year ended December 31, 2001 that are included in this prospectus. On June 18, 2002 we dismissed Arthur Andersen LLP and on July 10, 2002 appointed PricewaterhouseCoopers LLP as our independent registered public accounting firm.

Arthur Andersen LLP has not reissued its audit report with respect to the audited financial statements included in this prospectus covered by such report. Furthermore, Arthur Andersen LLP has not consented to the inclusion or incorporation by reference of its audit report in the registration statement of which this prospectus forms a part or in any other filings we may make with the SEC. As a result, investors in this offering may not have an effective remedy against Arthur Andersen LLP in connection with a material misstatement or omission with respect to our audited financial statements that are included elsewhere in this prospectus, the registration statement of which this prospectus forms a part or any other filing we may make with the SEC, including any claim under Sections 11 and 12 of the Securities Act of 1933, as amended. Even if such investors were able to assert such a claim, as a result of its conviction and other lawsuits, Arthur Andersen LLP may fail or otherwise have insufficient assets to satisfy claims made by investors or by us that might arise under federal securities laws or otherwise relating to any alleged material misstatement or omission with respect to our audited financial statements. In addition, in connection with any future capital markets transaction in which we are required to include financial statements that were audited by Arthur Andersen LLP, as a result of the foregoing, investors may elect not to participate in any such offering or, in the alternate, may require us to obtain a new audit with respect to previously audited financial statements. Consequently, our financing costs may increase or we may miss attractive capital market opportunities.

FORWARD-LOOKING STATEMENTS

We make forward-looking statements in this prospectus, including certain information set forth in the sections entitled Prospectus Summary, Business and Management s Discussion and Analysis of Financial Condition and Results of Operations. We have based these forward-looking statements on our current views and assumptions about future events and our future financial performance. You can generally identify forward-looking statements by the appearance in such a statement of words like anticipate, believe, continue, could, estimate, expe intend, may, plan, potential, predict, project, should or will or other comparable words or the negative of these words. When you co forward-looking statements, you should keep in mind the risk factors we describe and other cautionary statements we make in this prospectus.

Among the risks, uncertainties and assumptions to which these forward-looking statements may be subject are:

- our ability to have success in the clinical development of our technologies, including Progenta and Androxal;
- uncertainty related to our patent portfolio and the possibility of competing patents;
- our ability to raise additional capital after this offering on acceptable terms or at all;
- the reliability of clinical trials in non-U.S. jurisdictions;
- our ability to have Progenta and Androxal manufactured in amounts necessary for our clinical trials at an acceptable cost;
- our ability to remain listed on the Nasdaq SmallCap Market; and
- our ability to have success in meeting governmental regulations and the costs and time required to meet such regulatory requirements.

Our forward-looking statements are only predictions based on expectations that we believe are reasonable. Actual events or results may differ materially from those described in any forward-looking statement. We undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. To the extent these risks, uncertainties and assumptions give

rise to events that vary from our expectations, the forward-looking events discussed in this prospectus may not occur.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately $ l million (based on the last reported sale price of our common stock on October 18, 2004) from the sale of 4,000,000 shares in this offering, after deducting the underwriting discount and estimated offering expenses. If the underwriter s over-allotment option is exercised in full, we estimate that we will receive an additional $ l million. We intend to use the proceeds to continue clinical development of our Progenta and Androxal product candidates. In addition, we may use a portion of the net proceeds for working capital and general corporate purposes. Pending these uses, the net proceeds will be invested in investment-grade, interest-bearing securities. We believe such proceeds, together with our current resources, will last through the end of 2005. Thereafter, we anticipate additional financings to fund continued development and potential commercialization of our product candidates.

DIVIDEND POLICY

We currently intend to retain any future earnings to finance the growth, development and expansion of our business. Accordingly, we do not intend to declare or pay any dividends on our common stock for the foreseeable future. The declaration, payment and amount of future dividends, if any, will be at the sole discretion of our board of directors after taking into account various factors, including our financial condition, results of operations, cash flow from operations, current and anticipated capital requirements and expansion plans, the income tax laws then in effect and the requirements of Delaware corporate law.

PRICE RANGE OF COMMON STOCK

Our common stock is quoted on the Nasdaq SmallCap Market under the symbol ZONA and on the Pacific Stock Exchange under the symbol ZNG. The following table shows the high and low sale prices per share of our common stock, as reported by the Nasdaq SmallCap Market, during the periods presented.

	Price Range	
	High	**Low**
2002		
First Quarter	$7.44	$4.12
Second Quarter	4.68	0.90
Third Quarter	1.54	0.99
Fourth Quarter	1.42	0.75
2003		
First Quarter	$1.20	$0.87
Second Quarter	1.73	1.15
Third Quarter	1.97	1.28
Fourth Quarter	1.91	1.50
2004		
First Quarter	$4.35	$1.83
Second Quarter	5.40	2.44
Third Quarter	5.95	2.76
Fourth Quarter (through October 19, 2004)	3.93	3.30

All of the foregoing prices reflect interdealer quotations, without retail mark-up, markdowns or commissions, and may not necessarily represent actual transactions in our common stock.

On October 19, 2004, the last sale price of our common stock, as reported by the Nasdaq SmallCap Market, was $3.71 per share. On October 19, 2004, there were 207 holders of record of our common stock.

CAPITALIZATION

The following table sets forth our unaudited actual and as adjusted capitalization at September 30, 2004. The as adjusted column gives effect to the sale of 4,000,000 newly issued shares of common stock in this offering, based on an offering price of $ l per share (the closing price on l , 2004) and the receipt of net proceeds of approximately $ l after deducting the underwriting discount and estimated offering expenses payable by us. The actual price at which shares will be sold pursuant to this offering may be more or less than $ l per share, and such variation would affect portions of the as adjusted column of the following table. Depending on the extent of such variation, the effect on the as adjusted column could be material.

	September 30, 2004	
	Actual	As Adjusted
	(Unaudited)	(Unaudited)
Stockholders equity:		
Undesignated preferred stock, $.001 par value: 5,000,000 shares authorized; none issued and outstanding		
Common stock, $.001 par value: 20,000,000 shares authorized, 11,989,936 shares issued (actual) and 15,989,936 shares issued (as adjusted); and 4,992,901 shares outstanding (actual) and 8,992,901 shares outstanding (as adjusted)	$ 12	$
Additional paid-in capital	114,377	
Deferred compensation	(260)	(260)
Cost of treasury stock, 6,997,035 shares	(21,487)	(21,487)
Deficit accumulated during the development stage	(86,011)	(86,011)
Total stockholders equity	$ 6,631	$

The number of shares of common stock immediately outstanding after this offering is based on 4,992,901 shares outstanding as of September 30, 2004 on an actual basis and excludes:

1,836,846 shares of common stock issuable upon exercise of stock options at a weighted average exercise price of $4.84 per share;

381,933 shares available for grant under our 2004 stock option plan and 2000 director plan; and

127,366 shares of common stock reserved for future issuance under our 2000 employee stock purchase plan.

DILUTION

Our net tangible book value as of September 30, 2004, was approximately $6.3 million, or $1.25 per share. Net tangible book value per share represents our tangible net worth (tangible assets less total liabilities) divided by the total number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share that investors will pay in this offering and the net tangible book value per share immediately afterwards.

After giving effect to the receipt of $ l million of estimated net proceeds from the sale of 4,000,000 shares of our common stock in this offering at an assumed price of $ l per share after deducting the underwriting discount and estimated expenses of this offering, our adjusted net tangible book value as of September 30, 2004 would have been $ l million or $ l per share. This represents an immediate increase in our net tangible book value of $ l per share to existing stockholders and an immediate dilution of $ l per share to new investors purchasing our common stock in this offering. The following table illustrates this per share dilution to new investors purchasing our common stock in this offering:

Assumed public offering price per share		$
Net tangible book value per share as of September 30, 2004	$1.25	
Increase in net tangible book value per share attributable to new investors		
Adjusted net tangible book value per share after this offering		
Dilution per share to new investors		$

Assuming the exercise in full of the underwriter s over-allotment option, the adjusted net tangible book value per share after this offering would be $ l , the increase in net tangible book value per share to existing stockholders would be $ l and the dilution in net tangible book value per share to new investors would be $ l .

The table above also assumes no issuance of shares under options outstanding as of September 30, 2004. Upon completion of this offering, 1,836,846 shares of our common stock will be issuable upon the exercise of options granted under our stock option plans at a weighted average exercise price of $4.84 per share. Of these shares, l will be issuable under options that will be exercisable upon completion of this offering, with the remaining l becoming issuable at various intervals in the future based on remaining option vesting schedules. Please read Principal Stockholders for more information regarding outstanding options to purchase our common stock. If the l shares subject to options that will be exercisable upon completion of this offering were included in the above calculations, the dilution per share to new investors would be $ l , and if all 1,836,846 shares subject to options outstanding upon completion of this offering were included in the above calculations, the dilution per share to new investors would be $ l .

The following table illustrates, on an as adjusted basis as of September 30, 2004, the difference between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by the new investors purchasing shares of common stock in this offering, before deduction of the underwriting discount and estimated expenses of this offering payable by us.

	Shares Purchased		Total Cash Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	4,992,901	55.5%	$43,264,038	%	$8.67
New investors	4,000,000	44.5			
Total	8,992,901	100.0%	$	%	

If the underwriter exercises its over-allotment option in full, the shares held by existing stockholders will decrease to 1 % of the total number of shares of common stock outstanding after this offering, and the number of shares held by new investors will increase to 4,600,000, or 1 % of the total number of shares of common stock outstanding after this offering.

SELECTED CONSOLIDATED FINANCIAL INFORMATION

The statements of operations data for the three years ended December 31, 2003, 2002 and 2001 and the balance sheet data as of December 31, 2002 and 2003 have been derived from our audited financial statements included elsewhere in this prospectus. The statements of operations data for the nine months ended September 30, 2003 and 2004 and the balance sheet data as of September 30, 2004 have been derived from our unaudited financial statements included elsewhere in this prospectus, and, in the opinion of management, have been prepared on a basis consistent with the audited financial statements and include all adjustments, which consist only of normal recurring adjustments, necessary to present fairly in all material respects the information included in those statements. The statements of operations data for the years ended December 31, 1999 and 2000 and the balance sheet data as of December 31, 1999, 2000, and 2001 have been derived from audited financial statements not included in this prospectus. Our historical results are not necessarily indicative of results to be expected for any future period. The data presented below have been derived from financial statements that have been prepared in accordance with generally accepted accounting principles and should be read in conjunction with our financial statements, including the notes, and with Management s Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus.

	For the Year Ended December 31,					Nine Months Ended September 30,	
	1999	2000	2001	2002	2003	2003	2004
	(In thousands except per share amounts)						
Revenues and other income							
Licensing fees		$2,115	$2,162	$4,228			
Products royalties	$ 242	164	58				
Research and development grants		72	115	315	$ 595	$459	$118
Interest income	2,170	2,239	1,526	711	318	254	75
Gain on disposal of fixed assets					102	102	
Other income					35		
Total revenues and other income	2,412	4,590	3,861	5,254	1,015	815	228
Expenses							
Research and development	12,180	4,495	3,028	6,420	2,161		