KERYX BIOPHARMACEUTICALS INC
Form 8-K
December 30, 2005

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

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FORM 8-K

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CURRENT REPORT
Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of report (Date of earliest event reported): December 27, 2005

Keryx Biopharmaceuticals, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	**000-30929**	**13-4087132**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

750 Lexington Avenue
New York, New York 10022
(Address of Principal Executive Offices)

(212) 531-5965
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

£ Written communications pursuant to Rule 425 under the Securities Act.
£ Soliciting material pursuant to Rule 14a-12 under the Exchange Act.
£ Pre-commencement communications pursuant to Rule 14d-2b under the Exchange Act.
£ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act.

Item 1.01. Entry into a Material Definitive Agreement.

On December 27, 2005, the Compensation Committee of the Board of Directors of Keryx Biopharmaceuticals, Inc. (the "Company") approved base salaries for fiscal 2006 for each named executive officer. The table below indicates each named executive officer's base salary for fiscal 2006:

Executive officer	Base salary for 2006
Michael S. Weiss, Chairman and Chief Executive Officer	$ 375,000
I. Craig Henderson, President	$ 300,000
Ron Bentsur, Vice President, Finance and Investor Relations	$ 225,000(1)

(1) As previously announced, Mr. Bentsur has accepted the position of Chief Executive Officer of XTL Biopharmaceuticals, Ltd. He will remain as Vice President, Finance and Investor Relations of the Company until a successor is named. As a result, his base salary will be prorated in accordance with the amount of time he dedicates to his position at the Company.

Item 8.01. Other Events.

(a) Rule 10b5-1 Plan

On December 30, 2005, Michael S. Weiss, Chairman and Chief Executive Officer of the Company, adopted a Rule 10b5-1 trading plan (the "Plan") with a brokerage firm to exercise stock options issued to Mr. Weiss pursuant to his employment agreement and the Company's stock option plans and to sell the common stock underlying such options. Mr. Weiss entered into the Plan to facilitate the exercise of stock options and as part of his personal long-term investment strategy for asset diversification and liquidity. Mr. Weiss will have no control over the timing of the option exercises or stock sales under the Plan.

Pursuant to the Plan, the brokerage firm may exercise employee stock options of up to 1,000,000 shares of common stock (representing approximately 15% of Mr. Weiss's holdings) beginning in February 2006. The Plan is scheduled to terminate in February 2008, whether or not the total number of shares is sold. The stock options will be exercised monthly and the shares of common stock will be sold on a monthly basis pursuant to the following formula:

Share price on date of sale	Number of shares to be sold in month
$0 - $7.49	0
$7.50 - $12.49	10,000
$12.50 - $17.49	40,000
$17.50 - $22.49	80,000
Equal to or greater than $22.50	120,000

Any transactions under the Plan will be reported by Mr. Weiss through Form 4 filings with the Securities and Exchange Commission (the "SEC"). The Plan is intended to comply with Rule 10b5-1 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the Company's insider trading policy.

(b) Annual Report for the year ended December 31, 2004 on Form 10-K

As part of the the SEC's regular review of reports filed under the Exchange Act, the SEC requested that the Company revise the disclosure provided in its annual report on Form 10-K regarding the Company's significant assumptions used in valuing in-process research and development and the estimated costs and time to complete the current stage of

the Company's products under development.

The Company and the SEC agreed that such disclosure would be made in the Company's annual report on a going forward basis and that the Company would also file the disclosure on a Form 8-K to make the revised disclosure immediately available to investors. References to the relevant section of Form 10-K have been made for each disclosure item for the reader's convenience.

Revised Disclosure for the "Critical Accounting Policies" portion of the Management's Discussion and Analysis of Financial Condition and Results of Operations section of the Company's annual report on Form 10-K (Item 7):

Accounting Related to the Valuation of Acquired In-Process Research and Development.

As required by Financial Accounting Standards Board Interpretation No. 4, "Applicability of Financial Accounting Standards Board Statement No. 2 to Business Combinations Accounted for by the Purchase Method," or FIN 4, we recorded a charge of $18,800,000 for the estimate of the portion of the ACCESS Oncology, Inc., or ACCESS Oncology, purchase price allocated to acquired in-process research and development.

A project-by-project valuation using the guidance in Statement of Financial Accounting Standards No. 141, "Business Combinations" and the AICPA Practice Aid "Assets Acquired in a Business Combination to Be Used In Research and Development Activities: A Focus on Software, Electronic Devices and Pharmaceutical Industries" was performed with the assistance of independent valuation specialists to determine the fair value of research and development projects of ACCESS Oncology which were in-process, but not yet completed.

The fair value was determined using the income approach on a project-by-project basis. This method starts with a forecast of the expected future net cash flows. These cash flows are then adjusted to present value by applying an appropriate discount rate that reflects the project's stage of completion and other risk factors. These other risk factors can include the nature of the product, the scientific data associated with the technology, the current patent situation and market competition.

The forecast of future cash flows required the following assumptions to be made:

- revenue that is likely to result from specific in-process research and development projects, including estimated patient populations, estimated selling prices, estimated market penetration and estimated market share and year-over-year growth rates over the product life cycles;
- cost of sales related to the potential products using industry data or other sources of market data;
- sales and marketing expense using industry data or other market data;
- general and administrative expenses; and
- research and development expenses.

The valuations are based on information that was available as of the acquisition date and the expectations and assumptions deemed reasonable by our management. No assurance can be given, however, that the underlying assumptions or events associated with such assets will occur as projected. For example, the following changes in our assumptions would have yielded the indicated change in the total amount of the acquired in-process research and development charge:

- if the growth rate regarding the revenue assumptions for the three drugs under development and included in the assumptions on future cash flows were increased by 10%, the result on the aggregate amount of the charge would have been approximately $4,500,000, yielding a total charge of approximately $23,300,000, or if the growth rate were decreased by 5%, the result on the aggregate amount of the charge would have been approximately $2,200,000, yielding a total charge of approximately $16,600,000;
- if the discount rate used to bring the estimated future cash flows to a present value amount (which was based on a 55% rate) were reduced by 10%, the total charge would have increased to approximately $33,000,000, and if the discount rate were increased by 10%, the total charge would have decreased to approximately $11,000,000.

Additionally, if it was assumed that the research and development activity of the least developed of the three drugs under development acquired with ACCESS Oncology was going to be terminated for any reason and had no alternative future use, including inconclusive clinical results, the amount of the in-process research and development charge would have been reduced, possibly creating a situation where the Company would have recognized goodwill.

In each of the above scenarios, the change in the in-process research and development charge would have required an equal change in contingent equity rights, or if a significant decrease, goodwill would have been recorded. Contingent equity rights represent the lesser of negative goodwill and the maximum value of the contingent consideration at the date of the acquisition. Changes in the acquired in-process research and development charge do not change the amount or the value of the contingent consideration that could ultimately be paid.

Additional Disclosure for the "Overview" portion of the Management's Discussion and Analysis of Financial Condition and Results of Operations section of the Company's annual report on Form 10-K (Item 7):

Research and development expenses consist primarily of salaries and related personnel costs, fees paid to consultants and outside service providers for clinical and laboratory development, facilities-related and other expenses relating to the design, development, testing, and enhancement of our product candidates and technologies, as well as expenses related to in-licensing of new product candidates. We expense our research and development costs as they are incurred. Other research and development expenses, which excludes non-cash compensation and acquired in-process research and development expenses, for the years ended December 31, 2004, 2003 and 2002 were $9,805,000, $5,996,000 and $9,523,000, respectively.

The following table sets forth the other research and development expenses per project for the periods presented.

	Years ended December 31,			Cumulative, as of December 31,
	2004	**2003**	**2002**	**2004**
KRX-101	$ 6,064,000	$ 2,074,000	$ 2,215,000	$ 14,204,000
KRX-0401	2,230,000	N/A	N/A	2,230,000
Other clinical stage oncology compounds	623,000	N/A	N/A	623,000
Other	888,000	3,922,000	7,308,000	22,655,000
Total	$ 9,805,000	$ 5,996,000	$ 9,523,000	$ 39,712,000

Revised Disclosure for the "Products Under Development" portion of the Business section of the Company's annual report on Form 10-K (Item 1):

PRODUCTS UNDER DEVELOPMENT

KRX-101

Overview

Our lead compound under development is KRX-101 (sulodexide). We own the exclusive rights to use KRX-101 for the treatment of diabetic nephropathy in North America, Japan and certain other markets outside of Europe. Diabetic nephropathy is a long-term complication of diabetes in which the kidneys are progressively damaged. KRX-101, our lead drug candidate, is a glycosaminoglycan compound with structural similarities to the broad family of marketed heparins and low molecular weight heparins. Specifically, KRX-101 is comprised of heparan sulfate, also referred to as fast-moving heparin, dermatan sulfate and slow-moving heparin. This drug has been marketed in a number of European, Asian and South American countries for many years by our licensor for certain cardiovascular conditions and has a well established safety profile at the doses used for such indications. Additionally, it has been demonstrated in multiple clinical trials conducted in Europe and the U.S., including two randomized, double-blind, placebo-controlled Phase II studies, that KRX-101 can reduce urinary protein excretion in patients with diabetic nephropathy. KRX-101 is in a pivotal Phase III and Phase IV clinical program under a Special Protocol Assessment, or SPA, with the Food & Drug Administration, or FDA. These trials are being conducted by the Collaborative Study Group, or the CSG, the world's largest standing renal clinical trial group.

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We plan to develop KRX-101 in the United States, and possibly other countries where we have exclusive rights under our license, for the treatment of diabetic nephropathy and potentially for other indications.

Market Opportunity

According to the American Diabetes Association, or the ADA, there are 18.2 million people in the United States, or approximately 6.3% of the population, who have diabetes. Of this population, approximately 13 million have been diagnosed, of whom approximately 90-95% have been diagnosed with Type II diabetes. Type II diabetes results from the combination of insulin deficiency and the body's relative insensitivity to the insulin present, as opposed to Type I diabetes, in which severe insulin deficiency results from destruction of the insulin-producing beta cells of the pancreas. Moreover, an August 2003 study published by Datamonitor estimates that approximately 50% of all diabetics in the U.S., or approximately nine million people, have diabetic nephropathy. Diabetes is the most common cause of End Stage Renal Disease, or ESRD, in the United States and in many other developed nations and represents approximately 45% of all new cases of ESRD in the United States. Despite advances in clinical care, including improvements in glycemic or blood sugar control and blood pressure control, the number of Type I and Type II diabetes-related cases of ESRD continues to rise. In particular, the incidence of Type II diabetes-related ESRD is rapidly increasing. Approximately 20% of diabetics on dialysis in the United States survive for five years, making the mortality of end-stage renal failure in this group higher than most forms of cancer. Unfortunately, renal transplantation is an option for less than 15% of diabetics with ESRD, as compared to 35-40% of non-diabetics, principally due to age and concomitant vascular disease. Despite recent advances, diabetic nephropathy remains a potentially catastrophic illness for which partial but insufficient treatment is currently available.

Scientific Background

Both Type I and Type II diabetes are characterized by insufficient insulin effect upon insulin-requiring tissues. As insulin is required for normal metabolism of glucose, fat and protein, diabetes is accompanied by abnormal blood levels of these substances. In the short term, hyperglycemia, or elevated blood glucose, causes the classic symptoms of diabetes: excessive thirst, frequent urination and weight loss. In the long term, hyperglycemia, as well as other effects resulting from insufficient insulin effect, can progressively damage critical anatomic structures resulting in chronic diabetic complications. We are developing KRX-101 for the treatment of diabetic nephropathy, a long-term complication of diabetes in which the kidneys are progressively damaged. This progressive damage results in diminished kidney function progressing to ESRD, which ultimately leads to death unless treated by dialysis and/or renal transplant.

The kidney consists of two anatomically and functionally distinct components placed in serial configuration. The first component is the glomerulus, which performs the critical filtering function of the kidney. Blood is passed through delicate microscopic glomerular capillary loops, which, acting as sieves, allow waste chemicals and excess water to pass through into the glomerular filtrate while retaining desirable components, such as blood cells and albumin, within the blood. One of the key components of the glomerular capillary filtering membrane is highly anionic, or negatively charged, glycosaminoglycan molecules that are similar to the chemical components of KRX-101. The glomerular filtrate, which is the precursor of what will eventually be excreted as urine, flows into the next serial component, the tubular interstitial structure. In the tubules, further water is extracted from the filtrate and minerals and other body chemicals are absorbed from or secreted into the filtrate.

In diabetic nephropathy, it is the delicate glomerular loops that first sustain damage as a result of the diabetic state. These harmful effects include:

· The delicate filtering membranes of the glomerular loops thicken and their crucial anionic glycosaminoglycan molecules are either depleted or altered and lose some or all of their negative charge. As the glycosaminoglycan negative charge provides normal filtering selectivity to the glomerular membranes, their loss of negative charge results in the release of protein, usually albumin, from the blood into the filtrate and urine. The releases of abnormal amounts of protein or albumin into the urine are called proteinuria and albuminuria, respectively.

· In addition, hyperglycemia induced overproduction of TGF beta, a regulatory protein, by the kidney induces scar formation in the area surrounding the glomerular capillaries. Over time, the extrinsic pressure of this scar tissue causes collapse of individual glomeruli, loss of functionality and release of albumin into the filtrate and urine.

In normally functioning kidneys, interstitial structures are not exposed to albumin. It is believed that the exposure of the interstitial structures to albumin ultimately leads to a potent inflammatory and scarring response (mediated in part by TGF beta) in the tubules, as well as in the surrounding interstitial tissues. This scarring results in progressive diminution in kidney function. As might be expected, increasing urinary albumin excretion closely parallels this drop in kidney function. In ESRD, kidney function declines to the point where dialysis or transplantation becomes necessary to sustain life.

KRX-101 belongs to a proposed new class of nephroprotective, or kidney protecting, drugs, known as the glycosaminoglycans. A variety of members of this chemical family have been shown to decrease pathological albumin excretion in diabetic nephropathy in humans. Some of the members of this chemical family include the following approved drugs: standard heparin, low molecular weight heparin and danaparoid. However, these agents all require therapy by injection and are all potent anticoagulants, which are blood thinners capable of inducing bleeding. KRX-101, on the other hand, is given orally and, in this form, has demonstrated little, if any, anticoagulant effects to date.

Pre-Clinical and Clinical Data

Pre-Clinical Data

In pre-clinical studies, glycosaminoglycan components similar or identical to those that make up KRX-101 have been evaluated using well accepted rodent models of diabetic nephropathy, in both preventive protocols where the drug was given at a time when diabetes was induced and prior to kidney damage, and treatment protocols, where the drug was given after diabetic kidney damage was already present. These glycosaminoglycans diminished the thickening of glomerular capillary filtering membranes, replenished the crucial anionic, or albumin repelling, charge, lowered urinary albumin leakage and decreased kidney expression of the specific scar protein collagen IV, both in the preventive and the treatment protocols, returning these parameters nearly to their normal levels. In addition, data demonstrated that KRX-101 suppresses the hyperglycemia-induced, or high glucose-induced, overproduction of TGF beta, one of the most specific inducers of kidney scarring in diabetic and other kidney diseases. Thus, glycosaminoglycans similar or identical to the components of KRX-101 in pre-clinical models have prevented or reversed the hallmark “upstream” pathological abnormalities that drive the engine of progressive kidney dysfunction. Furthermore, data was presented at the 2005 American Society of Nephrology’s Renal Week that demonstrated that KRX-101 inhibited heparanase, an enzyme that is over-expressed in diabetic nephropathy patients and is believed to be a contributing factor to the long-term damage to the kidneys as a result of diabetes.

European Clinical Data

There have been approximately 20 studies published assessing the safety and efficacy of KRX-101 in humans. KRX-101 has been administered to more than 3,000 patients in clinical trials conducted in Europe for the treatment of certain diabetic and non-diabetic conditions and, to our knowledge, has not demonstrated any significant side effects at the doses tested for those uses.

European researchers, with the support of a grant by Alfa Wassermann S.p.A., or Alpha Wasserman, the licensor of KRX-101, conducted a randomized, double-blind, placebo-controlled, Phase II study of the use of KRX-101 to treat diabetic nephropathy in 223 patients in Europe between 1996 and 1999. In this study, also known as the DiNAS study, Type I and Type II diabetics with diabetic nephropathy were treated daily for four months with 50, 100 and 200 milligram gelcaps of KRX-101. These patients showed substantial dose-dependent reduction in proteinuria or pathological urinary albumin excretion rates. In this study, the higher the dose administered daily, the greater the demonstrated decrease in albumin excretion. The DiNAS study was published in the June 2002 issue of the Journal of the American Society of Nephrology.

U.S.-based Clinical Data

Our recently completed, U.S.-based Phase II multi-center clinical trial study was conducted by the CSG. This randomized, double-blind, placebo-controlled study compared two doses (200mg and 400mg daily) of KRX-101 versus placebo for the treatment of diabetic nephropathy in 149 patients between 2003 and 2005. We announced the positive results of this study at the American Society of Nephrology’s Renal Week in November 2005. Interim positive results from this study had been previously announced at the National Kidney Foundation’s Spring Clinical Meeting in May 2005. The results of the study are presented below.

Design of the Phase II Study

The Phase II study was designed as a pilot for the fully-powered pivotal Phase III study, which is currently ongoing. In this Phase II study, two doses of KRX-101 (200 mg and 400 mg) were compared to placebo in patients with diabetic microalbuminuria on maximal therapy with an angiotensin converting enzyme inhibitor, called an ACEi, or a angiotensin receptor blocker, known as an ARB. Patients were treated with KRX-101 or placebo for six months and followed for an additional two months post-treatment. Patients were randomized 1:1:1, placebo, 200mg and 400mg of KRX-101, respectively.

In this Phase II study, the primary endpoint for the study was the percentage of patients achieving "Therapeutic Success" at six months. This is also the endpoint in the protocol for the KRX-101 Phase III clinical trial now recruiting patients, and which was agreed to with the FDA under a SPA. A patient is considered a "Therapeutic Success" if they achieve one of the following outcomes following the six months in the study:

(1) 50% reduction in albumin to creatinine ratio or "ACR"— ACR is a standard measurement used to assess the level of kidney disease in these patients. ACR measures the level of albumin protein in urine, also referred to as "albuminuria," or

(2) Normalization of ACR with at least a 25% reduction in ACR—in this study the normal laboratory range for albuminuria was defined as less than 20mg of albumin to 1g of creatinine.

Phase II Data Analysis

A total of 149 patients were randomized into the study. All patients evaluable for Therapeutic Success at six months (i.e. all patients with a baseline ACR and a six-month ACR) were included in the Intent to Treat analysis, for a total of 136 patients. All patients in the Intent to Treat population that at baseline were within the target eligibility range of microalbuminuria as defined in the protocol (ACR 20mg/G to 200mg/G) were included in the Per Protocol analysis, for a total population of 117 patients.

All of the primary and secondary analyses shown were pre-specified. For the primary endpoint analysis, statistical nominal p values have been provided for informational purposes only since this Phase II study, as a pilot study, had less than a 20% power to show statistically significant results for these endpoints.

The data is being presented in two ways. First, the 200mg arm is compared to placebo because the 200mg is the dose in our Phase III and Phase IV protocols, as agreed to with the FDA under the SPA. Next, the data is presented as Active (200mg and 400mg) vs. Placebo; this was the primary endpoint defined by the Phase II protocol. Information on the effects of the 400mg arm alone can be found in the footnotes to the tables. The dose response relationship of KRX-101 previously demonstrated up to 200mg was not observed from 200mg to 400mg in this study.

Table 1—Primary Endpoint Analysis (Therapeutic Success at six months) (200mg vs. Placebo)

	Number of Patients (Placebo/200mg)	Placebo	200mg	p value Fisher's Exact Test (2-sided)
Per Protocol	36/36	11.0%	33.0%	P=.045
Intent to Treat	42/44	14.0%	32.0%	P=.074

Table 2—Primary Endpoint Analysis (Therapeutic Success at six months) (200mg and 400mg[1] vs. Placebo)

	Number of Patients (Placebo/Active)	Placebo	Active (200mg and 400mg)[1]	p value Fisher's Exact Test (2-sided)
Per Protocol	36/81	11%	25%	P=.136
Intent to Treat	42/94	14%	26%	P=.180

1 For the 400mg group alone, the Therapeutic Success was 18% on a per protocol basis and 20% on intent to treat basis.

Table 3—Secondary Endpoint Analysis at Six months (Intent to Treat)

	Placebo	200mg	Active (200mg and 400mg[1])
	n=42	n=44	n=94
>50 % reduction in ACR	12.0%	27.0%	22.0%
Normalization of ACR	9.0%	23.0%	17.0%

1 For the 400mg group alone, the 50% reduction and normalization were 18% and 10%, respectively.

Table 4—Average Changes of ACR Over Time (Intent to Treat[1])

	200mg vs. Placebo	Placebo vs. Baseline	200mg vs. Baseline
Two months	-17.00%	-4.0%	-21.00%
Four months	-25.78%	7.5%	-18.28%
Six months	-28.03%	12.57%	-15.46%
Eight months (Two months off therapy)	-28.98%	18.5%	-10.48%

1 The average changes from baseline over time for the 400mg dose group were 3.4%, 3.24%, 5.59% and 12.59%, respectively.

There were no serious adverse events, or SAEs, that were deemed by the investigators to be related, probably related or possibly related to the study drug. A full analysis of the safety database will be conducted in the coming months.

Development Status

In June 2000, we filed an investigational new drug application, or IND, with the FDA for permission to conduct a clinical trial for the treatment of patients with diabetic nephropathy. In 2001, KRX-101 was granted Fast-Track designation for the treatment of diabetic nephropathy, and, in 2002, we announced that the FDA had agreed, in principle, to permit us to avail ourselves of the accelerated approval process under subpart H of the FDA's regulations governing applications for the approval to market a new drug. Generally, subpart H allows for the use of surrogate endpoints in Phase III trials to support the approval of an NDA with confirmatory studies completed post-approval, and could greatly reduce the development time to market.

In the fourth quarter of 2003, we initiated the Phase II portion of our Phase II/III clinical program for KRX-101, and in the third quarter of 2004, we completed the target enrollment for the Phase II portion of the clinical program.

In January 2005, we announced that the CSG recommended that we proceed to the Phase III portion of our Phase II/III clinical program of KRX-101. This recommendation was based on the completion, by an independent Data Safety Monitoring Committee, or DSMC, on January 4, 2005, of a safety evaluation of the first interim analysis from the 149 patient, randomized, double-blind, placebo-controlled Phase II clinical trial of KRX-101 discussed above, and an efficacy assessment of the same data set conducted by the CSG.

In March 2005, we announced that we had finalized a SPA agreement with the FDA for the Phase III and Phase IV clinical trials of KRX-101.

In June 2005, we announced the initiation of our pivotal Phase III and Phase IV clinical program for KRX-101. We are conducting both of these trials under our SPA with the FDA. This clinical plan consists of: a single Phase III trial in patients with microalbuminuria based on the surrogate marker of regression of microalbuminuria as the primary endpoint; supportive data from previously conducted clinical studies; and substantial recruitment into our Phase IV confirmatory study that will measure clinical outcomes in patients with overt nephropathy, or macroalbuminuria. The Phase III portion of the program is a randomized, double-blind, placebo-controlled study comparing a 200 milligram daily dose of KRX-101 versus a placebo in patients with persistent microalbuminuria. The Phase IV portion of the program is a randomized, double-blind, placebo-controlled study comparing a 200 milligram daily dose of KRX-101 versus a placebo in patients with persistent macroalbuminuria. The CSG is conducting the pivotal Phase III and Phase IV clinical program of KRX-101 for the treatment of diabetic nephropathy.

In November 2005, we announced positive final results from our Phase II study of KRX-101 for diabetic nephropathy at the American Society of Nephrology's Renal Week. As discussed in detail above, the Phase II study compared two oral doses of KRX-101, 200 and 400 milligrams, versus a placebo in patients with diabetic microalbuminuria who were receiving an ACE inhibitor or ARB. In this study, patients were treated with KRX-101 or a placebo for six months and were monitored for an additional two months post-treatment. The primary endpoint for the study was "therapeutic success" of the two dose levels combined versus a placebo at six months. Therapeutic success was a binary composite endpoint defined as: conversion from microalbuminuria to normoalbuminuria (with at least a 25% reduction in microalbuminuria) as measured by the ACR; or at least a 50% reduction in the ACR level relative to baseline.

KRX-0401

Overview

We are also developing KRX-0401 (perifosine), which is a novel, first-in-class, oral anti-cancer agent that modulates Akt, a protein in the body associated with tumor survival and growth, and a number of other key signal transduction pathways, including the JNK and MAPK pathways, which are pathways associated with programmed cell death, cell growth, cell differentiation and cell survival. This compound has demonstrated preliminary single agent anti-tumor activity and is currently in a Phase II clinical program where it is being studied both as a single agent and in combination with other anti-cancer treatments for multiple forms of cancer.

KRX-0401 is the prototype of a new group of anti-cancer drugs referred to as alkylphosphocholines that block proliferation and induce the apoptosis of cancer cells. This effect is relatively specific for cancer cells compared to normal cells. The mechanism of action for these drugs is not clear. They are known to modulate signaling in a number of pathways known to function abnormally during the development of cancer. One of the pathways inhibited by the alkylphosphocholines is Akt, a pathway associated with tumor survival and growth. Akt is considered to be one of the most important cancer targets being researched today.

In September 2002, ACCESS Oncology, which we acquired in February 2004, entered into an exclusive commercial license agreement with Zentaris AG, a wholly owned subsidiary of AEterna Zentaris Inc., to acquire a license to a series of U.S. and foreign patents and patent applications relating to the composition of matter and use of KRX-0401 in the treatment of cancer and other conditions. This license agreement covers the United States, Canada and Mexico.

Pre-Clinical and Clinical Data

In vitro, KRX-0401 inhibits the growth of a variety of human tumor cell lines and has substantial activity in vivo against a number of murine tumor models and human xenografts. In model systems the drug appears to be synergistic with radiotherapy and additive or synergistic with cytotoxics such as cisplatin, adriamycin, and cyclophosphamide. In these experiments, the combination regimens were superior to chemotherapy alone and were well tolerated.

Pre-clinical studies presented at the American Society of Hematology Annual Meeting in December 2005 demonstrated KRX-0401's potential utility in the treatment of multiple myeloma and possibly other forms of hematological tumors. These studies demonstrated that KRX-0401 has activity in a variety of in vitro and in vivo multiple myeloma models and is synergistic with a number of agents used in the treatment of multiple myeloma including bortezomib (Velcade®) and dexamethasone.

Six Phase I studies of KRX-0401 have been completed, three in Europe by Zentaris and three in the U.S. by the National Cancer Institute, or NCI, a department of the National Institutes of Health, or NIH, as part of a Cooperative Research and Development Agreement, or CRADA, and by the Company. These trials demonstrated that KRX-0401 can be safely given to humans with an acceptable toxicity profile and no observed myelosuppression, or bone marrow suppression. The dose limiting toxicity in the Phase I studies was gastrointestinal: nausea, vomiting and diarrhea. In addition, some patients experienced fatigue, especially with prolonged administration. In these Phase I studies, there was single agent activity as evidenced by two durable partial responses (one of which lasted more than six months and the other more than 18 months) out of 10 patients with previously treated, evaluable soft tissue sarcomas, a tumor type relatively unresponsive to chemotherapy. In addition 21 patients were considered by the investigators to have had disease stabilization for two or more months, including patients with sarcomas (2), prostate cancer (3), non-small cell lung cancer (2), breast cancer (2), colon cancer (2), melanoma (2), renal cancer (2), ovarian cancer (1), salivary gland cancer (1), mesothelioma (2) and hepatoma (2). The meaning of disease stabilization in an individual patient in a Phase I study is difficult to assess because the time to progression is variable and may give a false impression of stabilization in individual patients.

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The NCI has completed a number Phase II clinical trials studying KRX-0401 as a single agent, including studies in prostate, breast, head and neck and pancreatic cancers, as well as melanoma and sarcomas. In total, nine NCI clinical trials have been conducted across the six tumor types mentioned. The NCI and its collaborators have presented and/or published data from seven of their Phase II studies, including from Phase II studies involving prostate (2), sarcoma, head and neck, melanoma, pancreas and breast cancers. Findings from these studies led the investigators to conclude that the drug was safe and well-tolerated at the Phase II dose utilized. The studies used dosing schedules in which a large “bolus” dose was given on day one or once every 28 days followed by daily doses either continuously or on days two to 21 of a four-week cycle. Bolus doses ranged from 300 mg to 900 mg followed by daily doses of 100 - 150 mg. These studies confirm the safety profile of the bolus plus daily regimens, which had limited grade 3 and no grade 4 gastrointestinal toxicity, the dose limiting toxicity in most of the Phase I trials. However, studies using a single bolus dose of 600 mg to 900 mg on day one and continuous daily KRX-0401 at a dose of 100 mg per day appeared to be better tolerated than studies that used 150 mg per day on days two to 21 in each four-week cycle. In the one published Phase II sarcoma study, the investigators reported a partial response (greater than 50% decrease in tumor mass) as well as several disease stabilizations. With the responses seen in the Phase I trials, there are now three sarcoma patients with durable partial responses. This has led us to consider exploring additional studies in sarcoma. On the Phase II breast cancer study, the investigators scored three of 15 evaluable patients as having stable disease. One of these patients had measurable tumor regression which failed to reach the level of a partial response by the time the patient elected to withdraw from the study because of gastrointestinal toxicity. The breast cancer trial utilized the more toxic of the regimens employed in these NCI Phase II studies. In the melanoma trial published by the National Cancer Institute of Canada, one patient with a primary mucosal melanoma of the vagina and inguinal adenopathy had a 50% reduction in the size of the palpable nodes after 4 cycles but developed new disease after cycle 5.

In May 2005, we announced that Phase II data presented at the annual meeting of the American Society of Clinical Oncology in Orlando, Florida demonstrated the tolerability and potential efficacy of KRX-0401 in the treatment of patients with biochemically recurrent hormone-sensitive prostate cancer, or HSPC. The investigators concluded that KRX-0401 in the treatment of HSPC patients is feasible, well-tolerated and has been shown to reduce prostate-specific antigen, or PSA, levels in some patients. Because of its inhibitory effects on the Akt and related pathways, we believe that further studies of KRX-0401 in combination with androgen ablation and chemotherapy are warranted. In a second study published by investigators at the NCI, there were no radiographic responses or PSA declines of 50% or greater related to KRX-0401, but four patients had stable PSA values for 12 weeks or longer. Eleven of 14 patients, or 78%, in whom circulating tumor cells were measured pre- and post-treatment, showed a decreased number of circulating tumor cells after treatment.

Development Status

During the second quarter of 2004, we announced the initiation of a Phase II program utilizing KRX-0401 as a single agent and in combination with a number of standard anti-cancer therapies in multiple tumor types. To date, we have initiated a number of trials under this program, including single agent studies in lung cancer and sarcoma, and combination studies with a number of standard anti-cancer treatments, such as gemcitabine, paclitaxel, docetaxel, Herceptin® and endocrine therapy. We have also initiated an “all-comers” Phase II clinical trial evaluating KRX-0401 as a single-agent, administered either weekly or daily in a variety of tumor types. We plan to commence additional Phase II trials in 2006.

The ultimate clinical timeline, and consequent cost, for further development of KRX-0401 will depend, in part, on the successful completion of our Phase II trials, and ultimate approval by the FDA.

ADDITIONAL PRODUCT CANDIDATES

KRX-0402

KRX-0402 (O6-benzyl guanine or O6-BG) is a small molecule that was specifically designed to block the repair protein, AGT. AGT confers resistance to 06-alkylating agents, such as temozolomide and BCNU, that are commonly used to treat brain cancer, melanoma and non-Hodgkin's lymphoma. Recent research has shown that KRX-0402 can also potentiate the activity of other alkylating agents, such as cisplatinum and carboplatinum, through an as of yet unconfirmed mechanism. These drugs are some of the most widely used chemotherapy drugs and are commonly used to treat breast cancer, non-small cell lung cancer and ovarian cancer. Accordingly, we believe that KRX-0402 may have an important role in making cells more susceptible to the damaging effects of alkylating agents, and that KRX-0402 may have utility in the treatment of multiple forms of cancer. KRX-0402 is usually administered intravenously. To date, approximately 400 patients have received KRX-0402 in multiple clinical studies. Dose limiting toxicity for KRX-0402 in combination with chemotherapy was bone marrow suppression. KRX-0402 alone has no identified dose limiting toxicity. Currently, we have plans to conduct additional company-sponsored clinical trials for KRX-0402.

KRX-0403

During 2005, we terminated development of KRX-0403.

KRX-0404

KRX-0404, currently in pre-clinical development, is an alkylphosphocholine, but, in contrast to KRX-0401, it is suitable for intravenous administration.

KRX-0501

KRX-0501, currently in pre-clinical development, is an orally available small molecule in pre-clinical development with the potential to treat neurological disorders via its unique ability to enhance nerve growth factor, a naturally occurring protein which is essential in the development and survival of certain sympathetic and sensory neurons in both the central and peripheral nervous systems.

COSTS AND TIME TO COMPLETE PRODUCT DEVELOPMENT

The information below provides estimates regarding the costs associated with the completion of the current development phase and our current estimated range of the time that will be necessary to complete that development phase for KRX-101. We also have provided information with respect to our other drug candidates. We also direct your attention to the risk factors which could significantly affect our ability to meet these cost and time estimates found in this report in Item 1A under the heading "Risk Factors Associated with Our Product Development Efforts."

KRX-101 is currently in Phase III and Phase IV clinical trials. We estimate that the cost to complete the Phase III will be approximately $20 million to $30 million and we believe that the Phase III will be completed in 2007.

With respect to KRX-0401 and KRX-0402, we are unable to estimate the cost to complete the current phase of each drug and also unable to project a time for the completion of the current phase. Each of KRX-0401 and KRX-0402 are in Phase II studies. Phase II clinical trials are highly unpredictable and their length and results will vary based on patient enrollment, response rates in the trials, and the potential need for additional trials or increases in patients included, among other factors. Due to the nature of a Phase II and our inability to predict the results of such studies, we cannot estimate when such a program will end, and it is equally difficult to project the cost to complete such phase.

KRX-0404 and KRX-0501 are currently pre-clinical drug candidates. The timing and results of pre-clinical studies are highly unpredictable. Due to the nature of pre-clinical studies and our inability to predict the results of such studies, we cannot estimate when such pre-clinical development will end, and it is equally difficult to project the cost to complete such development.

Revised Disclosure for the "Risk Factors" portion of the Business section of the Company's annual report on Form 10-K (Item 1A):

***Risk Factors Associated with Our Product Development Efforts*.**

If we are unable to successfully complete our clinical trial programs, or if such clinical trials take longer to complete than we project, our ability to execute our current business strategy will be adversely affected.

Whether or not and how quickly we complete clinical trials is dependent in part upon the rate at which we are able to engage clinical trial sites and, thereafter, the rate of enrollment of patients. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the existence of competitive clinical trials, and whether existing or new drugs are approved for the indication we are studying. We are aware that other companies are planning clinical trials that will seek to enroll patients with the same diseases as we are studying. In addition, one of our current trials for KRX-101 is designed to continue until a pre-specified number of events have occurred to the patients enrolled. Trials such as this are subject to delays stemming from patient withdrawal and from lower than expected event rates and may also incur increased costs if enrollment is increased in order to achieve the desired number of events. If we experience delays in identifying and contracting with sites and/or in patient enrollment in our clinical trial programs, we may incur additional costs and delays in our development programs, and may not be able to complete our clinical trials on a cost-effective basis.

Additionally, we have finalized with the FDA our SPA regarding a subpart H clinical development plan for the clinical development of KRX-101 for diabetic nephropathy. This clinical plan consists of: a single Phase III trial in patients with microalbuminuria based on the surrogate marker of regression of microalbuminuria as the primary endpoint; supportive data from previously conducted clinical studies; and substantial recruitment into our Phase IV confirmatory study that will measure clinical outcomes in patients with overt nephropathy, or macroalbuminuria, before filing a NDA with the FDA. The subpart H process is complex and requires careful execution and no assurance can be given that we will be able to meet the requirements set forth in the SPA. Even if we meet those requirements, the FDA is not obligated to grant approval of our NDA for KRX-101. If the FDA approves KRX-101 for marketing on the basis of our SPA, our Phase IV clinical trial may yield insufficient efficacy data or give rise to safety concerns, which could result in withdrawal of such approval or could cause us to withdraw the product from the market. Many companies who have been granted the right to utilize an accelerated approval approach have failed to obtain approval. Moreover, negative or inconclusive results from the clinical trials we hope to conduct or adverse medical events could cause us to have to repeat or terminate the clinical trials. Accordingly, we may not be able to complete the clinical trials within an acceptable time frame, if at all.

If Our Drug Candidates Do Not Receive The Necessary Regulatory Approvals, We Will Be Unable To Commercialize Our Drug Candidates.

We have not received, and may never receive, regulatory approval for the commercial sale of any of our drug candidates. We will need to conduct significant additional research and human testing before we can apply for product approval with the FDA or with regulatory authorities of other countries. Pre-clinical testing and clinical development are long, expensive and uncertain processes. Satisfaction of regulatory requirements typically depends on the nature, complexity and novelty of the product and requires the expenditure of substantial resources. Data obtained from pre-clinical and clinical tests can be interpreted in different ways, which could delay, limit or prevent regulatory approval. It may take us many years to complete the testing of our drug candidates and failure can occur at any stage of this process. Negative or inconclusive results or medical events during a clinical trial could cause us to delay or terminate our development efforts.

Furthermore, interim results of preclinical or clinical studies do not necessarily predict their final results, and acceptable results in early studies might not be obtained in later studies. Drug candidates in the later stages of clinical development may fail to show the desired safety and efficacy traits despite having progressed through initial clinical testing. There can be no assurance that the results from the Phase III study will track the data from the Phase II study, or that the results from the Phase IV study will yield sufficient efficacy data. Moreover, the recommendation to move into our pivotal program, as well as the announced Phase II data, may not be indicative of results from future clinical trials and the risk remains that the pivotal program for KRX-101 may generate efficacy data that will be insufficient for the approval of the drug, or may raise safety concerns that may prevent approval of the drug.

Clinical trials also have a high risk of failure. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after achieving promising results in earlier trials. If we experience delays in the testing or approval process or if we need to perform more or larger clinical trials than originally planned, our financial results and the commercial prospects for our drug candidates may be materially impaired. In addition, we have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approval in the United States and abroad and, accordingly, may encounter unforeseen problems and delays in the approval process.

Because All Of Our Proprietary Technologies Are Licensed To Us By Third Parties, Termination Of These License Agreements Would Prevent Us From Developing Our Drug Candidates.

We do not own any of our drug candidates. We have licensed the patent rights to these drugs candidates from others. These license agreements require us to meet development or financing milestones and impose development and commercialization due diligence requirements on us. In addition, under these agreements, we must pay royalties on sales of products resulting from licensed technologies and pay the patent filing, prosecution and maintenance costs related to the licenses. If we do not meet our obligations in a timely manner or if we otherwise breach the terms of our license agreements, our licensors could terminate the agreements, and we would lose the rights to our drug candidates.

We Rely On Third Parties To Manufacture Our Products. If These Third Parties Do Not Successfully Manufacture Our Products, Our Business Will Be Harmed.

We have no experience in manufacturing products for clinical or commercial purposes and do not have any manufacturing facilities. We intend to continue, in whole or in part, to use third parties to manufacture our products for use in clinical trials and for future sales. We may not be able to enter into future third-party contract manufacturing agreements on acceptable terms to us, if at all.

Contract manufacturers often encounter difficulties in scaling up production, including problems involving production yields, quality control and assurance, shortage of qualified personnel, compliance with FDA and foreign regulations, production costs and development of advanced manufacturing techniques and process controls. Our third-party manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required by us to successfully produce and market our drug candidates. In addition, our contract manufacturers will be subject to ongoing periodic, unannounced inspections by the FDA and corresponding foreign governmental agencies to ensure strict compliance with, among other things, current good manufacturing practices, in addition to other governmental regulations and corresponding foreign standards. We will not have control over, other than by contract, third-party manufacturers' compliance with these regulations and standards. Switching or engaging multiple manufacturers may be difficult because the number of potential manufacturers is limited and, particularly in the case of KRX-101, the process by which multiple manufacturers make the drug substance must be identical at each manufacturing facility. It may be difficult for us to find and engage replacement or multiple manufacturers quickly and on terms acceptable to us, if at all. Moreover, if we need to change manufacturers, the FDA and corresponding foreign regulatory agencies must approve these manufacturers in advance, which will involve testing and additional inspections to ensure compliance with FDA and foreign regulations and standards.

If third-party manufacturers fail to deliver the required quantities of our drug candidates on a timely basis and at commercially reasonable prices, we will not be able to commercialize our products as planned.

We have entered into a relationship with a U.S.-based contract manufacturer for KRX-101 which we believe will be adequate to satisfy our current clinical and initial commercial supply needs; however, as we scale-up for commercial manufacturing, we will need to ensure that the manufacturing process matches the established process on a larger scale. As with all heparin-like compounds, the end product is highly sensitive to the manufacturing process utilized. Accordingly, as we scale-up, reproducibility will be required for the successful commercialization of KRX-101. There can be no assurance that we will be successful in this endeavor. Additionally, as we scale-up, we will incur capital expenditures to enable larger scale production.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Keryx Biopharmaceuticals, Inc.
(Registrant)

Date: December 30, 2005

By: /s/ Ron Bentsur

Ron Bentsur
Vice President, Finance and Investor Relations