EXECUTIVE INFORMATIONAL OVERVIEW

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Novel Peptide-Focused Biotechnology Opportunity

Snapshot

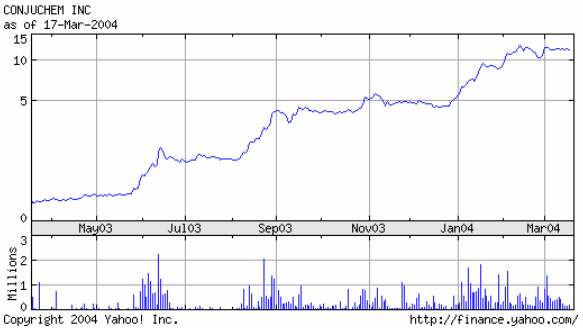
March 17, 2004

ConjuChem, Inc. is a Montreal-based biotechnology company focused on discovering and developing new drugs based on its novel technology platform called Drug Affinity Construct (DAC™). When applied to a compound, DAC™ can create a new drug with similar therapeutic activity but a significantly longer duration of activity in the body. One of the greatest opportunities for ConjuChem's DAC™ technology is its ability to harness the profound therapeutic potential of peptides, which are hindered by a variety of limitations. In particular, peptides have short durations of ***in vivo*** activity caused by their rapid degradation and elimination from the blood stream. This not only decreases their efficacy, but can also hold back their commercialization potential. ConjuChem's DAC™ technology, which is administered through **subcutaneous (SC)** injection but can also be administered **intravenously (IV)** or **intramuscularly (IM)**, is targeted towards novel therapeutics or new chemical entities (NCEs) in the areas of diabetes, growth hormone deficiencies, human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), and **congestive heart failure**.

Recent Financial Data

Ticker (Exchange)[1]	CJC.TO (TSX)
Recent Price (03/17/04)	$11.85
52-Week Range	$12.88-0.30
Shares Outstanding (mm)	41.5
Market Cap. (mm)	$491.8
Average 3-month vol.	454,271
Institutional Owners	85%
EPS (as of 01/31/04)	($0.20)
Employees	52

[1] *Amounts are in U.S. dollars.*



Key Points

NOTE: Unless otherwise stated within text, all dollars are expressed in Canadian dollars (CD).

- ConjuChem's most advanced development candidate, DAC™:GLP-1 (glucagon-like peptide), is being developed to treat patients with Type 2 diabetes. It appears to be ideal for controlling blood glucose by acting through several mechanisms of action and is unique since it only requires administration once every few days versus the several times per day required by nearly all other treatments under development using this mechanism of action.
- Phase I/II clinical trials for DAC™:GLP-1, presented at the American Diabetes Association and International Diabetes Federation 2003 meetings, achieved all primary endpoints. The Company estimates that the U.S. market for Type 2 diabetes treatments is approximately $6 billion, encompassing 15 million patients and growing.
- Due to the broad potential applications of the DAC™ technology—including diabetes, growth hormone deficiencies, HIV/AIDS, and congestive heart failure—ConjuChem actively seeks partnerships with companies engaged in both early and late stage drug development.
- The Company has recently completed an equity financing, providing it with a solid cash position of $40 million, or 18 months of cash with which to fund its development.

†**BOLD** WORDS IN TEXT ARE REFERENCED IN GLOSSARY ON PAGES 39-41.

Table of Contents

Executive Overview

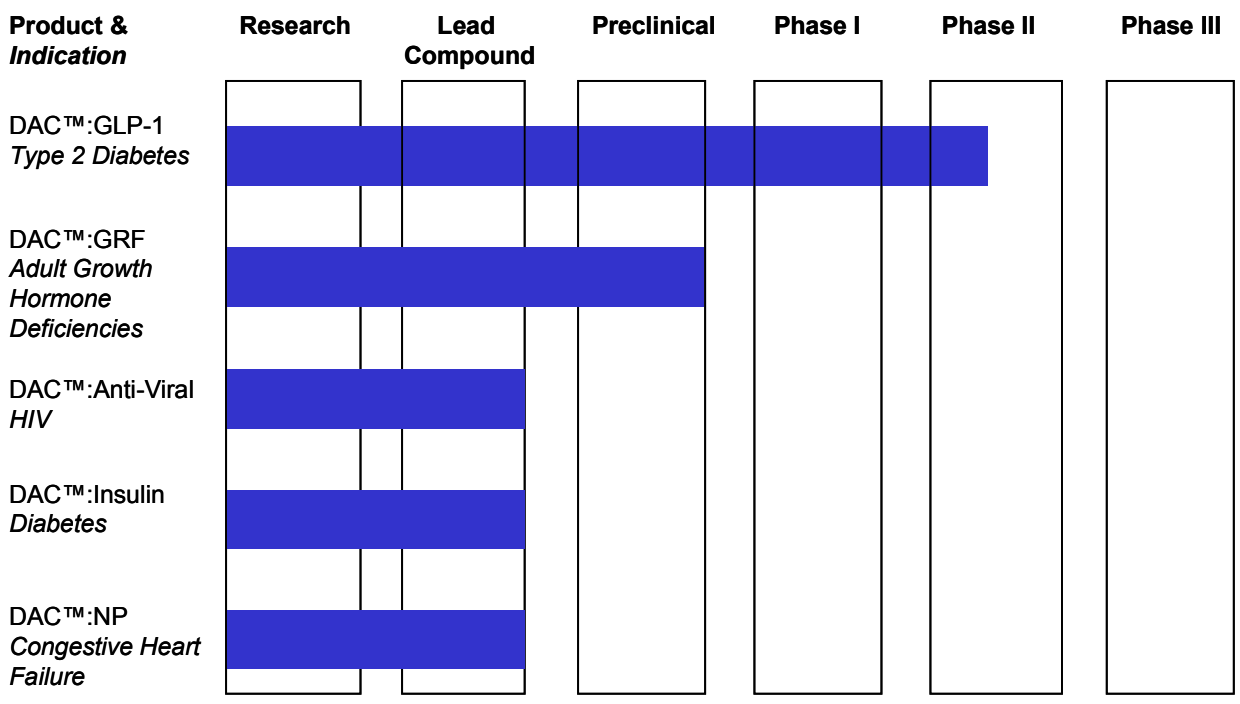
NOTE: Unless otherwise stated within text, all dollars are expressed in Canadian dollars (CD).

ConjuChem, Inc. is a Montreal-based biotechnology company focused on discovering and developing new therapeutic drugs based on its novel *in vivo* bio-conjugation technology. The Company's technology platform focuses on a drug construct called Drug Affinity Construct (DAC™), which, when applied to a compound, can create a new drug with similar therapeutic activity but a significantly longer duration of activity in the body and an enhanced safety profile.

One of the greatest opportunities for ConjuChem's DAC™ technology is its ability to harness the profound therapeutic potential of peptides, which are currently difficult to commercialize due to their short duration of *in vivo* activity caused by their **half-lives** of only a few minutes. Half-life is a measurement of the time needed for the plasma concentration or the amount of drug in the body to be reduced by 50%. Peptides are rapidly degraded by **enzymes** in the blood and excreted through the kidneys. These events not only decrease efficacy, but can also hinder a drug's commercialization potential. ConjuChem's DAC™ technology is designed to exploit the hidden potential of peptides by providing them with greater safety and longevity.

ConjuChem's DAC™ technology is targeted towards novel therapeutics or new chemical entities (NCEs) in the areas of diabetes, growth hormone deficiencies for multiple indications in children and adults, human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), and congestive heart failure. Figure 1 provides a snapshot of these areas of development and how far along they are within the pipeline. Extensive details are provided in the Core Story section on pages 10-28.

Figure 1
ConjuChem, Inc.
PIPELINE



Source: ConjuChem, Inc.

The Company's most advanced and lead development candidate, DAC™:GLP-1, is a derivative of glucagon-like peptide-1 for which encouraging Phase I/II data in Type II diabetes was reported at the American Diabetes Association and International Diabetes Federation meetings during the third quarter of 2003.

DAC™ constructs are composed of an active **moiety** (in particular, a peptide), a linker or connector, and a reactive chemistry to anchor *in vivo* the construct to **albumin**. DAC™ is administered subcutaneously but can also be administered by an intravenous (IV) or intramuscular (IM) injection. Once injected, the reactive chemistry portion will permanently bond to albumin, potentially offering significant improvements over the original drug moiety. Albumin is the most prevalent protein in the bloodstream, accounting for half the total protein content. DAC™ technology is also very flexible, allowing for modification in the length of the connector, the composition of the connector, and the sites of attachment.

ConjuChem believes that the following characteristics of albumin make the DAC™ technology a unique platform for developing pharmaceuticals:

- It is distributed throughout virtually all tissues in the body;
- It has a half-life of 15 to 20 days, supporting a highly favorable dosing regimen; and
- It does not readily cross the blood-brain barrier, minimizing the potential for central nervous system (CNS)-mediated side effects, such as addiction in the case of opioids.

Headquarters, Manufacturing, and Employees

ConjuChem was founded in 1997 following the acquisition of all the assets from the privately-held San Francisco-based firm, RedCell, Inc. The Company then came public on the Toronto Stock Exchange (TSX) in November 2000 when it successfully raised approximately $29 million upon issuing 4.55 million shares. ConjuChem currently employs 52 individuals, 14 of whom have Ph.D. or M.D. degrees. Approximately 80% of the employees are part of the Company's research and development (R&D) team. ConjuChem currently occupies 15,000 square feet of laboratory and office space at 225, President Kennedy Avenue, Suite 3950, Montreal, Quebec in a building owned by the University of Quebec at Montreal (UQAM). Its current lease expires in January 2005, with two additional two-year lease extensions available to the Company at its option.

Growth Strategy

ConjuChem has based its growth strategy on the anticipated success of its DAC™ technology. Using this technology, the Company has created novel drugs via a **bioconjugation process** involving the common plasma protein, albumin. DAC™ facilitates the creation of drug candidates with augmented half-lives by protecting the peptides from degradation and their elimination from the bloodstream and thereby maintaining therapeutic activity that is significantly longer than the parent drug from which it is derived.

The Company is currently using its DAC™ technology to develop the compounds described below.

- *DAC™:GLP-1 (Glucagon-Like Peptide) for treatment of Type 2 diabetes.* ConjuChem's most advanced compound in development, CJC-1131, is a patented GLP-1 analogue designed for subcutaneous administration. GLP-1 is a naturally-occurring peptide in the human body that offers many benefits for the treatment of Type 2 diabetes, such as the absence of weight gain or the incidence of hypoglycemia—two well-known side effects of the current diabetes treatments of **insulins** and sulfonylureas. The issue, however, is that the half-life of native GLP-1 is only a few minutes. While previous attempts to extend the half-life have successfully increased it from minutes to several hours, the drug still must be administered several times per day. Through DAC™ technology, ConjuChem is attempting to increase the half-life of the drug by binding GLP-1 covalently to albumin, thereby reducing the frequency of administration.

  The Company announced positive clinical results from two separate studies for this compound following the completion of a Phase I/II multidose clinical trial and a re-challenge study to assess the compound's absence of immunogenicity. The Phase I/II primary endpoints that were met were: (1) a statistically significant reduction in the average mean daily glucose level, (2) a statistically significant reduction in the fasting glucose level, and (3) the complete absence of adverse immune responses. The compound was also well tolerated by patients at all dosing levels. ConjuChem is currently initiating a large Phase II clinical program for GLP-1, enrolling up to 450 patients across Europe and North America. The objectives of this program are to further corroborate the early efficacy results achieved to date and to establish an optimal dosing regimen—potentially once per week for most patients—prior to entering the final stage of clinical development.

- *DAC™:GRF for treatment of growth hormone deficiencies.* ConjuChem's second program is aimed at the long-lasting production of natural pulses of growth hormone through weekly or biweekly administration of a non-growth hormone compound. DAC™: GRF could be developed to treat growth hormone deficiencies in critically ill adults such as burn victims and **sepsis** patients, **cachexia/lipodystrophy** (in particular in AIDS patients), and those with short stature. The technology has completed preclinical testing.

- *DAC™:Antiviral HIV.* During a research collaboration with the antiviral specialist, Tibotec, Inc., ConjuChem tested the concept of a DAC™:anti-HIV program. Positive preliminary data were obtained, but following the acquisition of Tibotec by Johnson & Johnson (JNJ-NYSE), the program was put on hold. ConjuChem is now pursuing work in this field on its own.

- *DAC™:Insulin.* ConjuChem is developing DAC™:Insulin as a component of diabetes therapy that would supply the basal level of insulin. DAC™ analogues have been synthesized and preliminarily tested in a variety of mouse and rat assays and have shown solid trends of activity, with glucose control for over six hours. Further work is ongoing.

- *DAC™:NP **(natriuretic peptide)** for treatment for congestive heart failure.* NP has shown a unique ability to relax the vascular smooth muscle, which leads to reduced blood pressure and thus reduced potential for congestive heart failure. The primary drawback of these peptides is their short half-lives in blood, making them less useful for the long-term management of the disorder. ConjuChem has several DAC™ derivative candidates that have demonstrated the ability to significantly improve the half-lives of the peptides. The technology is in the preclinical stage.

Intellectual Property

ConjuChem's patent portfolio is a key factor in assessing the value of the Company. ConjuChem expends a substantial amount of time and effort in managing and enriching its patent portfolio, working towards expanding its patent applications to all the major markets of the world. Patent protection is built around broad technology claims in addition to patents with specific compositions of matter, disease indications, manufacturing, process claims, and other embodiments.

ConjuChem currently has more than 170 patents pending and more than 30 patents issued on its DAC™ technology. The most mature of these patents, which expires in 2014, includes broad method claims for the use of *in vivo* bioconjugation for all therapeutic applications. Subsequent patent applications relate to specific therapeutic indications for novel drugs developed with the DAC™ technology. A snapshot of ConjuChem's key intellectual property portfolio is provided in Table 1.

Table 1
ConjuChem, Inc.
PATENT PORTFOLIO

Application Date	U.S Patent No.	Title
08/26/03	6,610,825	Method for alleviating pain or providing an analgesic effect in a patient
08/5/03	6,602,981	Antinociceptive agent derivative
07/15/03	6,593,295	Long lasting insulinotropic peptides
02/4/03	6,514,500	Long lasting synthetic glucagon like peptide {GLP-1}
12/31/02	6,500,918	Conjugate comprising an antinociceptive agent covalently bonded to a blood component
08/27/02	6,440,417	Antibodies to argatroban derivatives and their use in therapeutic and diagnostic treatments
08/20/02	6,437,092	Conjugates of opioids and endogenous carriers
06/11/02	6,403,324	Affinity labeling libraries with tagged leaving group
12/11/02	6,329,336	Long lasting insulinotropic peptides
08/21/01	6,277,863	Methods and compositions for producing novel conjugates of thrombin inhibitors and endogenous carriers resulting in anti-thrombins with extended lifetimes
08/21/01	6,277,583	Affinity labeling libraries and applications thereof
08/22/00	6,107,489	Extended lifetimes in vivo renin inhibitors
08/15/00	6,103,233	Cellular and serum protein anchors and conjugates
07/11/00	6,087,375	Methods of treating or preventing thromboses
08/24/99	5,942,620	Methods for producing novel conjugates of thrombin inhibitors

Source: U.S. Patent and Trademark Office.

Management and Board of Directors

Management

ConjuChem's management and scientific team contain individuals who are highly capable of driving the DAC™ technology from concept to commercialization and facilitating the creation of co-development and distribution partnerships. A snapshot of Company's management is provided in Table 2, followed by detailed biographies.

Table 2
ConjuChem, Inc.
MANAGEMENT

Jacques Lapointe	President, Chief Executive Officer
Jean-Paul Castaigne, M.D.	Vice President, Development and Chief Scientific Officer
Dominique P. Bridon, Ph.D.	Vice President, Research and Chief Technical Officer
Queenie Jang	Vice President, Corporate Development
Lennie Ryer	Vice President Finance, Chief Financial Officer
Pol-Henri Guivarc'h, M.D.	Vice President, Clinical Research and Development

Source: ConjuChem, Inc.

Jacques Lapointe, President and Chief Executive Officer

Mr. Lapointe is President and Chief Executive Officer of ConjuChem, having worked in the biotechnology and pharmaceutical sectors at senior levels for more than 30 years. His prior positions include President and Chief Executive Officer of Glaxo Wellcome Canada, as well as Glaxo Wellcome U.K. He was also a member of the Company's Worldwide Executive Committee, with responsibility for global business and commercial development. Previoulsy, Mr. Lapointe was President and Chief Operating Officer of BioChem Pharma Inc. Mr. Lapointe is also a board member for a number of other private and public companies.

Jean-Paul Castaigne, M.D., Vice President, Development and Chief Scientific Officer

Dr. Castaigne is Vice President, Development and Chief Scientific Officer of ConjuChem, having extensive international experience in top pharmaceutical companies. Prior to joining ConjuChem, he was Vice President, Head of Global Research & Development (R&D) at the Fournier Group in France for nearly two years. In addition, Dr. Castaigne spent 11 years with Novartis (NVS-NYSE) in a variety of management positions, including Vice President, Medical and Regulatory Affairs for Canada, President and Managing Director for Sandoz Phillippines, and Director of Medical and R&D for Sandoz in France. He received his M.D. from Paris University in 1975, held the position of Associate Professor of Oncology, Pneumology in 1978, and received his advanced diploma in Management of Business Administration in 1987 from the Commercial Chamber of Commerce of Paris. He is currently Honorary President of the Pharmaceutical Physician's Association in France.

Dominique P. Bridon, Ph.D., Vice President, Research and Chief Technical Officer

Dr. Bridon, Vice President, Research and Chief Technical Officer, is a co-founding Officer of ConjuChem. He has served ConjuChem as Vice President of Research since June 1997 and as Chief Technical Officer since May 2000. He previously served as Director of Biological Chemistry for Redcell, Inc. from 1996 to 1997. Over the seven-year period from 1989 through 1996, he held various scientific positions at Abbott Laboratories (ABT-NYSE) in the diagnostic and pharmaceutical research areas. Dr. Bridon has extensive experience in molecular design, chemical synthesis, and diagnostics development and has worked in the fields of bioinformatics and combinatorial chemistry. He has published in each of these areas and is an inventor with numerous patents. Dr. Bridon holds a doctorate in organic chemistry from

the University of Paris and did post-doctoral research in synthetic organic chemistry at the University of California, Berkeley. He has an engineering degree in polymer chemistry from Ecole Nationale Superieure d'Ingenieur in France.

Queenie Jang, Vice President, Corporate Development

Ms. Jang joined ConjuChem in June 1999 as Vice President, Corporate Development. Over the past 12 years, she has held a variety of senior management positions in business development, marketing, and strategy with Dupont Pharma, Sanofi-Synthelabo Inc. (SNY-NYSE), and Glaxo Wellcome, PLC (GSK-NYSE). In these roles, she led and directed the commercialization and launch strategies for a number of NCEs in migraine, thrombosis, and cardiovascular therapeutics. She has extensive experience in business development and has successfully negotiated a number of licensing, co-promotion, and joint venture agreements within the pharmaceutical and biotech industries. Ms. Jang has also served as a Principal with Ernst & Young Management Consulting in their Health Care and Life Sciences practice, focusing on the biotechnology sector. She holds an M.B.A. from the University of Western Ontario, Richard Ivey School of Business, and a Pharmacy degree from the University of British Columbia.

Lennie Ryer, Vice President Finance, Chief Financial Officer

Mr. Ryer is ConjuChem's Vice President, Finance and Chief Financial Officer. Prior to joining the Company, Mr. Ryer served as Chief Financial Officer and Vice President, Finance at Paladin Labs, Inc., (PLB-TSX) a specialty pharmaceutical firm. At Paladin, Mr. Ryer transitioned the company to the TSX. Mr. Ryer was formerly the Managing Partner of the Montreal office of BDO Dunwoody, an international firm of Chartered Accountants. During his 18 years in public practice, Mr. Ryer specialized in mergers and acquisitions and taxation. Mr. Ryer holds a B. Comm degree from McGill University and a degree in Public Accountancy from McGill University Faculty of Graduate Studies. He holds a Chartered Accountant designation from the Institutes of Ontario and Quebec, is a member of the Canadian Tax Foundation, and holds a designation as a Certified Fraud Examiner. Mr. Ryer assumes responsibility for the financial operations of ConjuChem and serves as the primary interface with the investment community.

Pol-Henri Guivarc'h, M.D., Vice President, Clinical Research and Development

Dr. Guivarc'h joined ConjuChem as Vice President of Clinical Research and Development in 2002. Dr. Guivarc'h was previously Vice President, Medical and Regulatory Affairs at SkyePharma Canada (previoulsy RTP Pharma), a drug delivery Company specializing in the formation of water-insoluble drugs with products in early clinical development at the registration stage. Dr. Guivarc'h brings to ConjuChem 17 years of successful industry experience in the conduct and management of clinical and regulatory drug development programs, including multinational pharmaceutical companies. He holds a Doctorate of Medicine from the University of Nice (France), a Computer Science degree form the University of Paris VI (France), and an M.B.A. from Concordia University, Montreal, Canada.

Board of Directors

Table 3 lists the Board of Directors of ConjuChem and their present principal occupation or management position in the Company. Mr. Felix J. Baker is a managing partner of Baker Biotech Fund I, L.P., Baker Biotech Fund II, L.P., Baker/Tisch Investments, L.P., Baker Bros. Investments I ,L.P. and Baker Bros. Investments II, L.P., which beneficially own, in the aggregate, 5,752,880 Common Shares and $24 million 7.07% convertible senior subordinated notes, the principal amount of which is convertible into up to an aggregate of 4,519,771 Common Shares at the option of the holder thereof at a conversion price of $5.31 per Common Share. Other Board members include Jacques Lapointe, who prior to 1998, was President and Chief Executive Officer of Glaxo Canada, Inc. and, prior to 2001, was President and Chief Operating Officer of BioChem Pharma Inc.; Nancy Lurker, who prior to 2003, was Group Vice President, Global Prescription Business, General Therapeutics II of Pharmacia; Steve Perrone, who prior to 2000, was Vice-President Finance and Chief Financial Officer of LGS Group Inc; Philippe Pouletty, who prior to 1998, was Chief Executive Officer of SangStat Medical Corporation (SANG-NASDAQ); and Claude Vezeau, who prior to 2002 was Partner and Vice President of BioCapital Management Group Inc., and prior to 1999, was President of BioChem Vaccines, a division of BioChem Pharma Inc.

Table 3
ConjuChem, Inc.
BOARD OF DIRECTORS

Name	Principal Occupation	Director Since
Felix Baker[1]	Managing Partner, Baker/Tisch Investments (life sciences investment fund)	2001
Jacques Lapointe[2]	Chairman, President and Chief Executive Officer, ConjuChem	2001
Nancy Lurker	President and Chief Executive Officer, Impact RX (pharmaceutical commercial effectiveness company)	2004
Steve Perrone[2]	Chief Financial Officer, Qbiogene Inc. (biotechnology company)	2002
Philippe Pouletty[1]	General Partner, Truffle Venture (investment fund)	1997
Claude Vezeau[1,2]	President and Chief Executive Officer, Innodia Inc. (biotechnology company)	2000

(1) Member of the Compensation Committee.

(2) Member of the Audit Committee.

Source: ConjuChem, Inc.

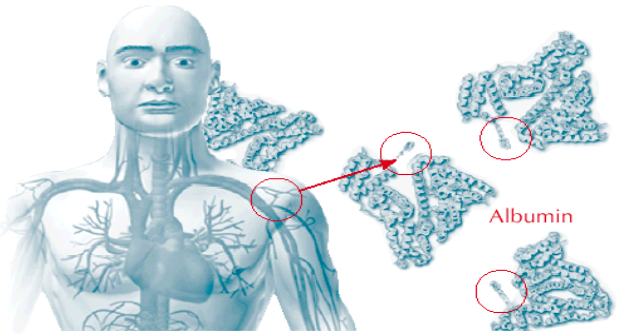
Core Story

DAC™ Technology Overview

Several companies are currently involved in efforts to extend the serum half-life of protein therapeutics by facilitating interaction with serum albumin. Other approaches are attempting to include a covalent drug attachment to blood cell surfaces or antibodies. In 2003, a German study in *Clinical Cancer Research* used albumin as a carrier for the common anti-cancer drug methotrexate. Another study published in 2002 in the *Journal of Medicinal Chemistry* described a chemically-reactive analog of another anti-cancer drug doxorubicin, which specifically binds to serum albumin at the same location as that targeted by ConjuChem's DAC™ constructs (see below). ConjuChem believes that these studies independently validate its DAC™ concept.

ConjuChem's DAC™ technology is designed to exploit the high therapeutic potential of peptides in order to treat a variety of disorders. Peptides have long been plagued by several biological drawbacks that have compromised their efficacy and, in many cases, hindered their ability to gain marketability. The principal drawback is a notably short duration of *in vivo* activity. Many peptides, following administration, have half-lives of only a few minutes, making repeated injections necessary for proper treatment. This is caused by their rapid enzymatic degradation in the bloodstream and excretion through the kidneys. ConjuChem believes that its DAC™ technology can protect peptides from these biological threats, making peptide-based therapies a more feasible and productive means of treatment with an enhanced safety profile.

Figure 2
ALBUMIN: THE IDEAL DAC™ CARRIER



Permanently bonds therapeutic drugs, specifically to albumin in the body.

The drug component maintains its original biological activity while adopting the disruption, excretion, and metabolism profile of albumin.

Albumin is the dominant protein in the blood.

Albumin circulates everywhere in the body.

Albumin has a long half-life of 19 days, supporting a highly favorable dosing regimen.

Albumin does not readily cross the blood-brain barrier, possessing few or no brain-related side effects, such as addiction.

Albumin is not primarily excreted through the kidneys or metabolized by the liver.

Source: ConjuChem, Inc.

ConjuChem's DAC™ technology is based on the following features:

- A synthetic modification of a well-characterized peptide moiety to yield a modified peptide **"predrug"** that contains a reactive chemical group though still retains most of its original biological activity. The modified peptide is called a Drug Affinity Construct or DAC™.
- The *in vivo* covalent attachment of the predrug is through reaction of the active moiety with the free thiol group of cysteine 34 in circulating albumin after **parenteral** administration to generate a bioconjugate. This bioconjugate is the active drug. The covalent attachment is permanent and the peptide will not be released from its albumin carrier to perform its biological function.
- Albumin performs the key operation of carrying the DAC™.

Albumin was chosen for the reasons described in Figure 2 (page 10). In vivo conjugation of the DAC™ predrug is highly selective as albumin is by far the most preeminent protein in the plasma and its single free thiol (cysteine 34) is highly reactive for the maleimide chemistry used. Furthermore, these benefits also make albumin a key contributor to the safety, durability, and productivity of DAC™.

Design of DAC™ Construct

Each DAC™ construct is composed of:

1. A drug component (small molecule or peptide), which is responsible for the biological activity of the compound inside the body.

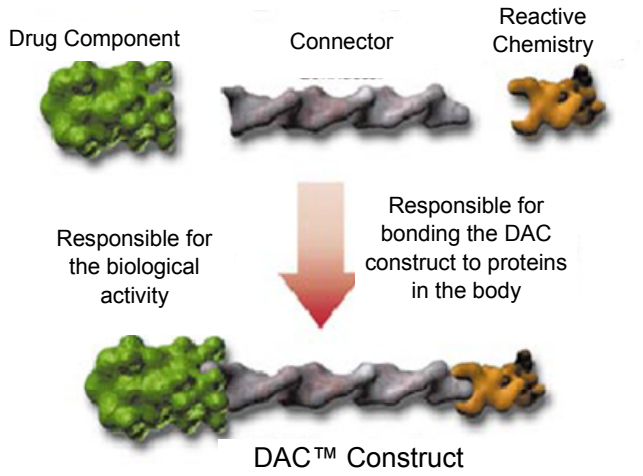
2. A linker or connector attached to the drug component, which binds the components together.

3. A reactive chemistry group at the opposite end of the linker. In particular, maleimide is used for its selective reactivity with the free thiol of albumin (cysteine 34).

This unique design allows ConjuChem to create a DAC™ construct that retains the therapeutic properties of the original drug, with higher biological activity (efficacy). Once DAC™ drug constructs are in the body, they have been shown to outperform the original drugs in terms of:

Figure 3

DRUG AFFINITY COMPLEX (DAC™) TECHNOLOGY



Source: ConjuChem, Inc.

- *Safety*. DAC™ drugs do not readily cross the blood brain barrier and thus are not likely to result in central nervous system (CNS)-mediated side effects.

- *Longevity.* Prior to DAC™ synthesis, most original drug compounds only lasted minutes in the body in their native form. DAC™ drugs can stay active in the body for days at a time.

Since one of the greatest benefits of ConjuChem's DAC™ technology is its ability to harness the profound therapeutic potential of peptides, which are currently difficult to commercialize due to rapid degradation in the human bloodstream, the Company has targeted its DAC™ technology towards existing drugs, therapeutic compounds in development, or compounds that have not been developed due to poor **pharmacokinetics**. Clinical studies have shown that the albumin-DAC™ drug bioconjugates can retain a level of potency similar to the original drug, while demonstrating both an improved circulating half-life and the distribution pattern of albumin in the body, including not-crossing the blood-brain barrier. Specifically, this technology is being directed towards multiple drugs in a variety of therapeutic fields, including diabetes, growth hormone deficiencies, HIV/AIDS, and congestive heart failure. Each of these conditions and their application to the DAC™ technology is described in the subsequent pages.

Human clinical data support a lack of immunogenicity following repeated challenges with a variety of DAC™ compounds. This is important since active immune responses could produce adverse events or contribute to reduced efficacy over time through the production of neutralizing antibodies and other cell-mediated immune events. Additionally, DAC™ technologies' flexibility could enable ConjuChem to apply rigorous criteria in choosing potential drug targets, thereby increasing the chances of developing a commercially feasible therapeutic. Type 2 diabetes is described in the following section along with ConjuChem's development efforts in this area with its DAC™ technology. Subsequently, we describe growth hormone deficiencies for multiple indications in children and adults as well as the application of the Company's DAC™ technology in treating these deficiencies. Descriptions of the Company's earlier stage development efforts are described on pages 26-28 under Preclinical Development Programs.

Type 2 Diabetes

Diabetic patients are classified into two types. In Type 1, the body does not produce insulin, while in Type 2, (the more common form of diabetes), the body does not generate enough insulin or is unable to use it properly. Insulin, which is produced by the **pancreas,** is a hormone that controls the level of the sugar glucose in the blood. As a result, insulin allows cells in the body to use glucose for energy. When the body is devoid of insulin, glucose builds up in the blood causing a condition called **hyperglycemia** or high blood glucose. To compensate, the pancreas produces more insulin. The cells, in order to stem the flood of insulin to the body, become more resistant, resulting in high glucose levels and, oftentimes, high insulin levels. Type 2 diabetes, consequently, places the human body at risk for a variety of long-term physical disorders, which are listed in Table 4.

Table 4

POTENTIAL PHYSICIAL DISORDERS ASSOCIATED WITH TYPE 2 DIABETES

Disorder	Description
Eye problems	Diabetes can have an adverse affect on the small blood vessels in the eyes. As the condition progresses, these blood vessels can become fragile or blocked, potentially damaging an individual's ability to see. Also called **retinopathy,** this visual disorder has no early symptoms, sometimes going undetected for long periods of time, necessitating yearly eye examinations and frequent monitoring.
Kidney disease	This condition, called **nephropathy**, occurs when diabetes damages the small blood vessels in the kidneys. While it has no early symptoms, nephropathy yields a variety of adverse effects on the body's ability to excrete waste products. It also inhibits the body from retaining valuable nutrients by flushing them away. As waste continues to build up in the bloodstream and the body is deprived of these nutrients, the possibility of kidney failure increases.
Nerve damage	Also called **neuropathy,** nerve damage is similar to blood vessel blockage. When blood pressure is high, nerve cells swell and scar, eventually losing their ability to send signals to the body. In many cases, the result is burning pain, numbness or loss of feeling in the feet and legs, sexual dysfunction, and changes in the stomach and bowel function.
Surgical loss	Improper circulation and nerve damage pose a high threat to the body's extremities. In many cases, an individual may be unaware that their body is infected or injured. Poor blood flow also hinders the body's ability to adequately perform the healing function and, in very serious cases, it may be necessary to surgically remove a foot or limb.
Frequent infection	Since high blood sugar levels can reduce the body's infection-fighting capabilities, individuals suffering from diabetes are predisposed to a variety of potential infections, such as the flu, skin infections, bladder infections, vaginal yeast infections, and tooth and gum infections.
Heart attack and stroke	One of most prevalent causes of death from Type 2 diabetes is a heart attack. Abnormal levels of blood fats, high blood pressure, and high blood sugar levels put individuals with the disorder at a much greater risk for heart attacks and strokes.

Source: Eli Lilly & Company.

Prevalence

Currently, at least one in every 16 U.S. citizens (6.2% of the population) suffers from diabetes. Of these cases nationwide, approximately 90-95% are Type 2 diabetes. Diabetes is also a somewhat covert condition. While an estimated 11.1 million people have been diagnosed with diabetes, approximately half as many, or 5.9 million people, are unaware that they have the disease. Additionally, this figure is quite large worldwide, with approximately 150 million people suffering from the disease. Women have a slightly higher risk of developing Type 2 diabetes than men, partially because they live longer.

While diabetes can affect all age groups, the disease is most common among individuals aged 65 or older, who account for nearly 40% of all cases. Ethnicity also appears to have an affect on risk. In general, the age-specific prevalence of diagnosed diabetes is higher for African Americans and Hispanics than for Caucasians. Among those younger than 75 years, African American women had the highest number of diagnosed diabetes cases.

The number of cases is also growing significantly. Between 1980 and 2000, the number of cases diagnosed grew from just under 6 million to over 11 million, according to the Centers for Disease Control and Prevention (CDC). Based on this trend, U.S. government researchers project that one in every three babies born in 2000 will develop the disease at some point in their life.

“Pre-diabetes” is also a concern to medical professionals. While individuals in the early preliminary stages of developing diabetes can still avoid contracting the disease, their risk of obtaining it is quite high. According to Dr. K.M. Venkat Narayan, M.D., Chief of Diabetes Epidemiology for the Centers for Disease Control and Prevention (CDC), approximately 16 million adults ages 40 to 74 have pre-diabetes.

Risk Factors

While there is no known cause of Type 2 diabetes, a variety of risk factors are recognized, which contribute to an individual’s risk of obtaining the disorder. These risk factors are listed in Table 5.

Table 5
RISK FACTORS FOR DEVELOPING DIABETES

Genetics and family history	Studies have confirmed that diabetes can be passed down genetically and can be inherited at birth. Since family history appears to contribute to diabetes, individuals with a known history of diabetes in their family are advised to undergo regular check-ups and stay highly aware of their blood sugar levels.
Race and ethnicity	African Americans, Hispanics, Native Americans, Asians, and Pacific Islanders have higher incidence of diabetes.
Weight	Approximately 75-80% of people with Type 2 diabetes are obese at the time of diagnosis.
Age	Individuals over 40 are at an increased risk for diabetes. This trend increases with age, as individuals above the age 65 account for more than 40% of all reported cases of diabetes in the United States.
Other	High blood pressure. The stress of an illness or injury. Giving birth to a child who weighs more than nine pounds.

Source: Eli Lilly & Company and CDC.

Symptoms and Diagnosis

Table 6 SYMPTOMS OF TYPE 2 DIABETES
fatigue
dry and itchy skin
numbness or tingling in hands and feet
frequent infections
increased urination
blurred vision
sexual dysfunction
slow healing of cuts or sores
increased hunger and thirst
weight loss
Source: Adam.com.

The early stages of Type 2 diabetes often have few to no symptoms, causing many individuals to go for long periods of time unaware of their condition. When symptoms do occur, they may surface gradually and subtly. Table 6 lists some of the primary symptoms of Type 2 diabetes.

The diagnosis of Type 2 diabetes occurs when:

- A fasting plasma glucose (FPG) level, which is measured by a blood test, is above 126 milligrams per deciliter (mg/dl) on two occasions;
- A random plasma glucose (PG) level is above 200 milligrams per deciliter with the symptoms of increased thirst, urination, and fatigue; and
- A PG level greater than 200 two hours after consuming a standardized carbohydrate beverage (Oral Glucose Tolerance Test or OGTT).

Treatment

Treating Type 2 diabetes requires the correct combination of physical activity, nutrition, pharmaceutical treatments, insulin treatments, and monitoring of blood-sugar levels. Patients with the disease are instructed to vigilantly monitor their condition and lead healthy lifestyles.

- *Exercise.* The first stage in treating diabetes is exercise. Physical activity helps the body burn off excess glucose as energy, reducing hyperglycemia and diabetic symptoms. Exercise has shown to improve blood glucose levels in older patients who otherwise suffered from high levels. Exercise also reduces the fatigue that often accompanies diabetes. Since many patients have not exercised for long periods of time, they are encouraged to begin with short, five-minute workouts and work their way up to longer workouts.
- *Diet.* Maintaining a healthy blood sugar level is highly dependent on the types of food a diabetic consumes. Since weight is such an important factor in the management of diabetes, diabetics must maintain a diet that enables them to remain at a healthy weight. Patients are encouraged to avoid skipping meals and follow a low-fat, low-salt, low-sugar meal plan. High fiber foods, such as beans, vegetables, and whole grains are also recommended.
- *Blood Glucose Monitoring.* Blood glucose monitoring enables patients to remain regularly informed of their blood glucose levels. The test, which is administered through a portable machine called a **glucometer**, can be performed at any time. It requires the finger to be pricked and placing a drop of blood on a reagent strip, which is composed of a chemical substance known to react in a specific way. A meter is then used to read the strip and display the result as a number on a digital display. This informs patients of the blood glucose level and enables them to respond with the appropriate intervention.
- *Insulin Treatments.* Nearly four out of 10 people with Type 2 diabetes take insulin. This naturally occurring hormone, which is secreted by the pancreas, enables the cells to use glucose from the blood. Since patients with Type 2 diabetes experience an inability to perform this function naturally, insulin therapies are employed. By increasing the uptake of glucose by the cells and alleviating the buildup of excess glucose in the blood, insulin plays a key role in preventing or reducing many of the long-term effects of diabetes, such as damage to the blood vessels, kidneys, eyes, and nerves.

- *Medications.* When diet and exercise do not sufficiently lower blood glucose levels, medication is introduced into the treatment plan. Available by prescription, diabetic medications perform distinctly different functions, alleviating a variety of symptoms associated with Type 2 diabetes. Table 7 provides a snapshot of some of the leading Type 2 diabetes medications on the market, their function, as well as potential side effects.

Table 7
TYPE 2 DIABETES MEDICATIONS

Product	Drug Class	Function	Side Effects
Amaryl® (glimepride) DiaBeta® (glyburide) Diabinese™(chlorpropamide) Glucontrol® (glipzide) Micronase® (glyburide) Tolinase® (tolazamide) Orinase® (tolbutamide)	Sulfonylureas	Trigger the pancreas to produce more insulin.	Hypoglycemia, weight gain, and water retention
Glucophage®	Biguanides (Metformin)	Inhibits the liver from producing glucose, decreasing glucose levels in the bloodstream.	anorexia, diarrhea, nausea, and abdominal discomfort
Prandin® (repaglinide)	Meglintides	Trigger the pancreas to produce more insulinin in response to glucose in the blood. Given before meals to regulate after-meal blood sugar levels.	Moderate weight gain and hypoglycemia
Precose®	Alpha-glucosidase inhibitors	Decrease the absorption of carbohydrates from the digestive tract, lowering the after-meal glucose levels.	Flatulence, diarrhea, and abdominal pain
Avandia® (rosiglitazone) Actos® (pioglitazone)	Thiazolidinediones PPAR Gamma Agonists	Enable insulin to work better at the cell site. This helps to increase the cell's ability to use insulin.	Fluid retention with edema occuring in 5% of patients
	Sulfonylurea and setformin, sulfonylurea and insulin, repaglinide and metformin, glyburide and metformin	Combination therapies	Variable

Sources: Avandia-side-effects.com, Ascensia Care, Yahoo Health.

It is important to note that a specific class of anti-diabetes drugs called PPAR (peroxisome proliferator-activitated receptor) gamma agonists has recently received a great deal of attention. One of the best-known of these, Avandia from Glaxo SmithKline, addresses Type 2 diabetes by enhancing the performance of the PPAR gamma, helping the body to make more efficient use of insulin. Since GLP-1 analogues stimulate the production and release of insulin and PPAR gamma agonists act to increase the hormone's action, these classes of drugs do not directly compete and combination therapy is possible.

GLP-1—A New Approach to Treating Type 2 Diabetes

A novel class of drugs is being developed that mimics the effects of the human insulinotropic hormone, called GLP-1 (Glucagon-Like peptide). GLP-1 is produced in response to food intake and controls glucose levels by stimulating the release and synthesis of insulin, by reducing glucagon secretion, and by controlling appetite. Mimics of GLP-1 act by binding to GLP-1 receptors on pancreatic beta cells and stimulating insulin secretion. These agents also suppress glucagon production, reduce appetite, and delay nutrient absorption from the stomach. This promotes the stimulation of insulin secretion when blood glucose levels are too high, but not during periods of normal or low blood-glucose concentrations. This process, unique to GLP-1, reduces the risk of hypoglycemia and also improves one's ability to manage weight.

GLP-1 is a peptide derived from **proglucagon**, a hormone secreted from the small and large intestines. Researchers believe that the hormone has the potential to ease a condition called **postprandial hyperglycemia**, which is a rapid rise in blood glucose that occurs after a meal. Research indicates that GLP-1 can decrease this condition by helping the pancreas release insulin and by slowing the movement of food out of the stomach. This is accomplished through targeting pancreatic basal cells. By promoting basal cell responsiveness, GLP-1 allows for the increased secretion of insulin from the pancreas, enabling cells to better use the energy from food.

Table 8
PRIMARY FUNCTIONS OF GLP-1

Increases insulin release in a glucose-dependent manner
Enhances insulin biosynthesis
Slows gastric emptying and acid secretion
Inhibits appetite and regulation of satiety setpoint
Decreases glucagon's secretion in a glucose dependent manner
Integrates glucose sensing and glucose clearance
Induces b-cell proliferation
Restores b-cell sensitivity to glucose

Source: ConjuChem, Inc.

Table 8 lists some of the primary functions of GLP-1. While GLP-1's various functions have the potential to be highly beneficial in treating Type 2 diabetes, the peptide's therapeutic ability is hindered by its remarkably short half-life. Since GLP-1 is only active for a shot time, many believe that the therapeutic capacity of the peptide will never be fully realized. However, methods are being explored to lengthen GLP-1's half-life and create GLP-1 derivatives with greater bioactivity and longer half-lives.

ConjuChem's DAC™:GLP-1 Analogue

DAC™:GLP-1 or CJC-1131, the lead candidate in ConjuChem's pipeline, is being developed as a prolonged treatment for Type 2 diabetes. This compound uses patented DAC™ technology to provide for an extended half-life. This reduces the need for frequent and inconvenient injections as required by the other analogues in development. ConjuChem's CJC-1131 is administered subcutaneously and is being developed as both a monotherapy and a combination therapy with other anti-diabetic agents (thiazolidinediones, biguanides, sulfonylureas, and glitinides) for Type 2 diabetes.

Preclinical Studies

Preclinical studies of CJC-1131demonstrated that it is effective in lowering basal blood glucose levels in diabetic db/db mice and blood glucose levels following an oral glucose tolerance test. In evaluating the half-life of the analogue, CJC-1131 demonstrated considerable improvement when tested in mice, rats, and dogs. Table 9 provides an overview of the demonstrated half-life of CJC-1131 in various mammals when administered both intravenously and subcutaneously.

Table 9
CJC-113 REPORTED HALF-LIFE
(DEMONSTRATED IN HOURS)

	Intravenous	Subcutaneous
Mice	17	23
Rats	20	21-25
Dogs	56	110

Source: ConjuChem, Inc.

Clinical Development

Positive clinical results from two separate studies of DAC™:GLP-1 were announced on August 21, 2003. The data come from the completion of a Phase I/II multidose clinical trial and a re-challenge study to assess the compound's absence of immunogenicity. Results showed that the following Phase I/II primary endpoints were met: (1) a statistically significant reduction in the average mean daily glucose level, (2) a statistically significant reduction in the fasting glucose level, and (3) the complete absence of adverse immune responses. The compound was also well tolerated by patients at all dosing levels.

Additionally, ConjuChem announced at the end of October 2003 the successful completion of a Phase I/II single dose trial with an IV formulation of DAC™:GLP-1. All primary endpoints were met. The study's safety, tolerability, and pharmacokinectic/pharmacodynamic parameters were consistent and similar to those reported from the subcutaneous administration in Phase I/II trials that were reported previously. The maximum tolerated dose (MTD) was not reached as a function of the drug being well tolerated, even at the highest dose level of 12 mcg/kg.

ConjuChem also announced in November 2003 that it had begun European enrollment in its first Phase II trial for DAC™:GLP-1. This monotherapy study will have data from no less than 150 evaluable diabetic patients and is designed to assess the reduction of the **HbA1c** (glycosylated hemoglobin A1c, a measure of average blood glucose over a 60-90 day period) level after three months of treatment and determine the optimum subcutaneous dosage regimen. Results from this study are expected before the end of June 2004.

Phase I/II Multidose Subcutaneous Trial Results

On August 21, 2003, ConjuChem reported that two separate studies of its DAC™:GLP-1 compound reached primary endpoints in Type 2 diabetes trials, allowing it to move rapidly into a Phase II clinical study. The study tested nine Type 2 diabetes patients (eight on drug and one on placebo). Each patient received the following subcutaneous administrations: 2 mcg/kg/day for 3 days, followed by 4 mcg/kg/day for the next 11 days (20 days total). All patients in the study were washed out of all their antidiabetic medications and received only DAC™:GLP-1 as a monotherapy. An overview of the key findings of the study is provided below.

- A highly statistically significant reduction of the average mean daily glucose level.
- A highly statistically significant reduction in fasting glucose level.
- Glucose normalization (according to ADA standards) or near normalization achieved in all patients in the fourth cohort.
- A long duration of activity. When measured seven days after the end of treatment, meal tolerance tests showed a marked statistically significant reduction of glucose excursions and an increase of meal-stimulated insulin levels.
- A statistically significant reduction of body weight, with the average body weight reduction being approximately 3 kilograms (6.6 pounds).

- In all studies to date, the compound has been well tolerated with no serious side effects and no injection site irritation. Consistent with side effects seen with other GLP-1 compounds, mild nausea and vomiting in some subjects were observed. However, a low oral dose of metoclopramide and/or induction of tachyphylaxis were able to effectively control these symptoms.

ConjuChem has commenced a Phase II clinical program that will enroll up to 450 patients across Europe and North America. This monotherapy study will have data from no less than 150 evaluable diabetic patients. The study is designed to assess the reduction of the HbA1c level after three months of treatment and determine the optimum subcutaneous dosage regimen. Results from this study are expected before the end of June 2004.

ConjuChem also announced the successful completion of a Phase I/II single dose trial with an intravenous (IV) formulation of DAC™:GLP-1. All primary endpoints were met. The study's safety, tolerability and pharmacokinectic/pharmacodynamic parameters were consistent and similar to those reported from the subcutaneous administration in Phase I/II trials that were reported on August 21, 2003. The MTD was not reached as a function of the drug being well tolerated, even at the highest dose level of 12 mcg/kg.

Immunogenicity Results. Specific immunogenicity results were derived from a total of 33 subjects (21 patients and 12 healthy volunteers) who were followed up to 70 days after receiving their last dosage. In the re-challenge study, 12 healthy volunteers previously exposed (six to 12 months prior to DAC™:GLP-1) received two re-challenge doses of 2 mcg/kg six weeks apart (similar protocol to a typical vaccination scenario). Both the initial exposure and the subsequent re-challenges were administered subcutaneously. In the multiple dose study, patients received the drug subcutaneously every day for up to 20 days and the 8 patients of the last cohort received a subcutaneous re-challenge dose one week after the end of the 20-day treatment period.

Key immunogenicity findings were:

- No signs of clinical immunogenicity
- No biological sign of immunogenicity
    - No specific IgG or IgE antibodies
    - No lymphocyte activation
    - No injection site reaction
    - No change in plasma concentration (no neutralizing antibodies).

CJC-1131 is currently in four Phase I/II clinical trials in the U.S. and Europe (see Table 10 on page 19). The first Phase I/II trial of the analogue began in July 2002, but was halted in September 2002 after 81 patients and volunteers were dosed, and the Company determined that the formulation used in the trial was inadequate. The trial resumed in February 2003 when an improved formulation was developed. Three additional Phase I/II trials have since commenced using a new formulation of CJC-1131.

ConjuChem is also conducting a Phase I/II trial of CJC-1131 for the treatment of hyperglycemia in hospitalized patients with acute conditions in the U.S. The Company was granted a pre-investigational new drug (IND) consultation with the Food and Drug Administration (FDA) in March 2003 and subsequently filed an IND authorizing initiation of the program. The IND was cleared by the FDA on April 29, 2003 and the first cohort of patients was dosed on May 27, 2003. In order to determine the most appropriate route of administration, ConjuChem has stated that it will test in parallel subcutaneous and intravenous methods. Table 11 on page 19 summaries the Company's clinical trial programs underway.

Table 10

CJC-1131 ONGOING PHASE I/II STUDIES

Trial	Description	Status	Comments
DM 100-001 Phase I/II, The Netherlands	Single dose SC in healthy volunteers and patients with type 2 diabetes (105 participants)	Ongoing (study resumed in February 2003 with a new drug product lot). Decision pending regarding additional patient cohort(s) with higher doses	Interim safety and pharmacokinetic results available. The Company plans to keep this trial open until it is determined that no higher dose is appropriate
DM 100-001 Phase I/II, The Netherlands	Multiple dose SC ascending dose in healthy volunteers and patients with Type 2 diabetes (27 to 36 participants)	Ongoing (trial started in March 2003)	Study to determine the tolerability, safety, and pharmacokinetic and preliminary efficacy parameters of 14-day administration
DM 100-002 Phase I/II, U.S.	Single dose IV in patients with Type 2 diabetes (30 patients)	Ongoing (trial started in May 2003)	5 groups with increasing doses at 2 week intervals. Clinical portion of the study to be completed in July
DM 100-041 Phase I/II, The Netherlands	Rechallenge study	The consecutive rechallenge 6 weeks apart of 15 healthy volunteers who were previously treated with CJC-1131; ongoing (started May 2003)	Immunogenic study

Source: ConjuChem, Inc.

Table 11

DAC™:GLP-1 DEVELOPMENT TIMELINE

Timeframe	Status	Details
Q1 2003	Initiated Phase I/II Trial	A robust study, with an enrollment potential of 110 people, including 52 diabetic patients
Q2 2003	Results Phase I/II Trial	Reliable endpoints will indicate early clinical efficacy and insight into the compound's therapeutic potential
Q2 2003	Initiated U.S. Clinical Trial	All diabetic patients IV administration is added to SC formulation
Q4 2003	Began European enrollment in Phase II	European clinical trial
Q4 2003	Results Phase I/II trial	U.S. clinical trial

Source: ConjuChem, Inc.

Competition

There are a variety of organizations that are currently researching and developing GLP-1 analogues. A snapshot of these organizations and their corresponding efforts are described below:

- *Amylin Pharmaceuticals—AC2592*. Amylin Pharmaceuticals (AMLN-NASDAQ) acquired a Phase II GLP-1 (7-36 amide) program as a congestive heart failure continuous infusion therapy plus various GLP-1 intellectual property assets from Restoragen in the first quarter of 2003.

- *Aventis SA/Zealand Pharma AS—ZP10*. Aventis SA (AVE-NYSE) announced a partnership with the Danish biotechnology firm, Zealand Pharma AS, in the second quarter 2003 to develop its GLP-1 analogue, ZP10. This peptide is a modified exendin-4 molecule with six additional lysine molecules attached to its C-terminus. This analog has already undergone Phase I/II testing showing that either once-daily or twice-daily administration reduces blood glucose levels in Type 2 diabetics for at least six weeks. A longer-acting ZP10 formulation based on Alkermes Inc.'s (ALKS-NASDAQ) Prolease technology is in early development.

- *Eli Lilly & Company/Amylin Pharmaceuticals—Exenatide or exendin-4*. Amylin and Eli Lilly & Company (LLY-NYSE) reported in the fourth quarter 2003 preliminary data from their three Phase III trials: after seven months of twice-daily injections some 40% of patients normalize to ≤7% their HBA1c. An average HBA1c reduction of 1% and weight-loss of 4-5 pounds were also noted. In these patients, blood glucose levels were not controlled either by metformin or sulfonylureas. A weekly or monthly injectable exenatide formulation based on Alkermes' Medisorb technology has been developed and a separate IND was filed in the first quarter 2003. Although Phase II pharmacokinetic data suggested that longer-term exenatide release is possible, formulation and manufacturing optimization is still ongoing. As exenatide is derived from a lizard, a high level of antibodies is developing in patients injected twice daily. So far, this has not impacted the efficacy or safety of the compound.

- *Human Genome Sciences—Albugon*. Human Genome Sciences Inc.'s (HGSI-NASDAQ.NM) albumin:GLP-1 fusion peptide has performed well in animal testing. The peptide has a half-life of 11 hours in mice and three days in monkeys, which is notably longer than the five-minute half-life of GLP-1 alone in humans, and restores near-normal blood glucose levels in diabetic animals. The Company acquired its albumin fusion technology upon purchasing Principia Pharmaceuticals in 2001 for US$120 million. Since then, the Company advanced albumin fusion proteins of interferon-alpha, interleukin-2, and growth hormone in early clinical trials.

- *Novo Nordisk A/S—NN2211*. Novo Nordisk A/S (NVO-NYSE) has attached fatty acids to peptide hormones to facilitate binding to albumin (protein lipidation), representing an alternative to ConjuChem's covalent albumin attachment via DAC™. NN2211 is a long-acting GLP-1 (7-37) derivative developed by Novo Nordisk and incorporates several changes to the native hormone: attachment of a C-16 fatty acid to the lateral chain of lysine 26 and replacement of the lysine 34 by an arginine. Clinical data on NN2211 were published in the July 2003 issue of *Diabetes* showing in a 20-patient study that a single NN2211 injection (7.5 micrograms/kg, which is within the range tested by ConjuChem in its DAC™:GLP-1 human studies to date), restored the ability of beta-cells in Type 2 diabetics to respond to high glucose levels. A separate 13-patient study showed that NN2211 daily administration for one week both enhanced insulin release and reduced blood glucose. NN2211 does not seem to impair glucagon release if patients become hypoglycemic, an important safety concern that the FDA will likely expect for DAC™:GLP-1 as well. The peptide is now in Phase II testing.

- *Novartis AG.* Novartis is developing LAF-237, an inhibitor of dipeptidyl peptidase IV (DPP-IV) for use in the treatment of Type 2 diabetes. This compound works by increasing the natural levels of GLP-1 by blocking the DPP-IV enzyme, which metabolizes GLP-1. Recently presented Phase II results demonstrated increased GLP-1 levels and improved HBA1c after 12 weeks.

- *Theratechnologies Inc.—ThGLP-1*. Theratechnologies Inc.'s (TH-TSX) long-acting peptide (LAP) platform protects enzymatic cleavage sites without modifying the peptidic sequence by adding a short hydrophobic pharmacophoric group. In the case of GLP-1(7-37), groups were added to the histidine 7, and data presented in June 2003. No precise structure has been released to date. The Company is also in early development stages of a transdermal GLP-1 formulation with Johnson & Johnson's Alza subsidiary.

Human Growth Hormone

Human growth is the result of a myriad of physical changes that occur throughout childhood and into the early years of adulthood. During the first year, a baby will nearly triple its birth weight. Following this dramatic year of growth, a general slowing occurs, which continues until puberty (age 11 in girls and age 13 in boys). Aside from the natural process, there are several additional factors that influence the human growth process, listed in Table 12.

Table 12
FACTORS INFLUENCING HUMAN GROWTH

Heredity	While still in the womb, a mother's size has a direct effect on the size and weight of a child. During the first 18 months, maternal and paternal characteristics become more apparent, with infants of tall parents more likely to grow faster than infants with shorter parents. A high correlation also exists between a child's eventual weight and height and the weight and height of his or her parents.
Nutrition	Maintaining a healthy diet is key for normal, healthy growth. If a child is malnourished during these key formative years, he or she has a higher risk for a reduced growth rate.
Hormones	A variety of hormones, acting like chemical messengers, are distributed and circulated throughout the bloodstream. Almost all hormones, which affect the activity of various cells, have some effect on a child's growth pattern.
Childhood Illness	Many childhood diseases can affect growth. Ailments that affect the heart and lungs as well as gastrointestinal disease can negatively impact growth.
Medications	Many medications used to treat childhood illnesses also have an adverse affect on growth. However, a change in dosage or discontinuation of the medication may result in a resumption of normal growth.

Source: Eli Lilly & Company.

Human Growth Hormone

Human growth hormone is a natural protein produced by the **pituitary gland** and transported through the bloodstream to specific target cells, which are located in key growth areas in the arm and leg bones. Composed of 191 amino acids, human growth hormone occurs at its highest levels in individuals who are not fully grown and diminishes with age. It also serves a key function in the kidneys, stimulating the liver's production of an insulin-like growth factor, IGF-1 hormone, which is the principal mediator of growth hormone released throughout the body. Human growth hormone's key functions in children and adults are as follows:

- Controls protein synthesis;
- Tells the body how fast to burn fat and calories; and
- Develops bone structure and muscle mass.

Growth Hormone Deficiency

While growth hormone serves distinct purposes in both children and adults, a deficiency of the hormone can cause a variety of adverse effects. There are several causes of growth hormone deficiency, with most related to a problem in the **hypothalamus**, an area of the brain that regulates body temperature, hunger, and thirst, or in the pituitary gland, which is directly responsible for the release of human growth hormone. In certain cases, growth hormone deficiency occurs as a result of the body's inability to use human growth hormone. Depending on age, size, and physical maturity, growth hormone deficiency increases an individual's vulnerability to several related dysfunctions. Tables 13 and 14 on page 23 provide an overview of growth hormone deficiency's effect on both adults and children.

Adults. While human growth hormone executes its primary function in an individual's early, formative years, adults need a healthy amount of human growth hormone as well. While growth hormone deficiency is less prevalent in fully-grown adults, Table 13 lists symptoms that are related to the disorder.

Table 13

SYMPTOMS RELATED TO HUMAN GROWTH HORMONE DEFICIENCY IN ADULTS

Excess fat stored, particularly in the abdomen, causing cholesterol levels to rise and resulting in a greater risk for heart attack and/or stroke
Reduced left ventricular mass in the heart, combined with decreased cardiac output
Increased arterial plaque and blood pressure
Reduced muscle mass, adversely affecting physical performance. Since this problem is directly associated with muscle mass, exercise will not correct the problem
Reduced energy and vitality, causing an individual to become fatigued and sluggish
Reduced bone mass, increasing the risk for fracture
Abnormal body composition, such as abdominal obesity and increased fat mass
Decreased social contact
Sleep depravity
Low blood sugar

Sources: Human Growth Foundation.

Children. Growth hormone deficiency is a common affliction of many children. Approximately one in every 10,000 children is born with growth hormone deficiency, with some countries reporting rates as high as one in 4,000. Due to its key role in the development and physical maturity of children, growth hormone deficiency manifests itself in a variety of ways, as listed in Table 14.

Table 14

MANIFESTATIONS OF GROWTH HORMONE DEFICIENCY IN CHILDREN

Growth in Height	Children with growth hormone deficiency grow at an abnormally slow rate, which becomes apparent by two to four years of age.
Head	While the body grows at a slow rate, head circumference increases normally.
Adiposity	Since growth hormone deficiency causes an inefficient breakdown of fats in the body, children with growth hormone deficiency have a notably higher level of adipose tissue, particularly around the waste.
Muscle development	Muscle development in children with growth hormone deficiency is notably lower than in normally developed children. This is evident through a lower amount of skeletal muscle cells, causing reduced strength.
Genitals	Male genitalia are underdeveloped, although normally functional.
Blood sugar levels	Children with growth hormone deficiency are at a higher risk for hypoglycemia and seizures due to an inadequate breakdown of glycogen into glucose.
Appearance and voice	Children with growth hormone deficiency will typically have a chubby appearance and high voice.

Source: Eli Lilly & Company.

Prevalence

Growth hormone deficiency affects approximately 70,000 adults, with about 10,000 to 15,000 children in the U.S. also exhibiting short stature due to growth hormone deficiency. Though most children (at least 95% or more) diagnosed with growth hormone deficiency receive treatment, only about 15% of diagnosed adults receive treatment. All but one of the commercial growth hormone therapies must be injected daily and, while generally effective, are often discontinued due to the inconvenience of this daily dosing. The only sustained-release formulation is not a panacea as half of the dose is released within the first 48 hours and the remainder over the next two to four weeks, which could explain the lower growth rates observed compared to the daily version. Furthermore, it results in mild to moderate injection-site reactions in nearly all patients.

Growth hormone deficiency increases the severity of multiple diseases, including but not limited to congenital deficiencies in children, AIDS-related lipodystrophy, chronic obstructive pulmonary disease (COPD), and slow recovery from injury in elderly patients. Children often experience problems with pituitary gland or hypothalamus development during embryogenesis and can exhibit congenital growth hormone deficiencies, or acquire chronic growth hormone deficiency-related conditions like Prader-Willi Syndrome (about one in 12,000 live births) or Turner Syndrome (about one in 2,000 live-born girls). Chronic renal insufficiency and thalassemia may also cause reduced growth hormone secretion.

Treatments

While several human growth hormone alternatives are available in an over-the-counter (OTC) pill or inhalation form, these therapies are notably less potent and are not as active in the body as some other pharmaceutical treatments. Currently, the most productive way to deliver human growth hormone therapy is through injection. Table 15 lists some of the common ethical treatments for growth hormone deficiencies.

Table 15

COMMON TREATMENTS FOR HUMAN GROWTH HORMONE DISORDERS

Norditropin	A synthesized form of somatropin, a synthetic or naturally occurring growth hormone. The primary reason for norditropin's popularity is its ease of delivery. The hormone is synthesized into a powder and comes in a ready-to-use form, making it the fastest way to introduce human growth hormone into the body in injectable form.
Genotropin	A synthesized, powder form of somatropin. The injectable form of this hormone is available in a two-chamber system. Since genotropin powder requires water to work, one chamber holds the powder, while the other holds the water. Upon injection, the water interacts with the powder and is delivered into the body.
Secretagogue	A human growth hormone enhancer available in pill or powder form. Secretagogues rarely have side effects and are available without prescription, costing anywhere from $30 to $200 per month. These enhancers work by supplementing the body with compounds known to increase the body's production of human growth hormone.
Human Growth Hormone Spray	These are liquid products administered under the tongue or sprayed through the nose or mouth. There is currently no proven legitimacy to these products, making their effectiveness questionable.

Source: HGH Station.

Competition and Market Opportunity

The existing worldwide market for growth hormone alone exceeded US$1.7 billion in 2002, with three leading brands alone accounting for US$800 million. In the U.S., Genentech Inc.'s (DNA-NYSE) Nutropin/Protropin, Pfizer Inc.'s (PFE-NYSE) Genotropin, Novo Nordisk's Norditropin, Serono SA's (SRA-NYSE) Saizen/Serostim/Zorbtive, and Eli Lilly's Humatrope are commercialized. Serono used to market a 29-amino acid amidated GRF fragment called sermorelin (Geref), but discontinued it in 2002. Serono has

a PEGylated GRF in Phase I clinical testing. Merck & Company (MRK-NYSE) is also testing an orally-active, non-peptidic growth hormone secretagogue MK-0677.

ConjuChem's DAC™:GRF Agonist

ConjuChem is currently developing a long-lasting GRF agonist to perform some of the key functions currently served by human growth hormone. The Company believes that a GRF agonist may show improved properties compared to some of the current human growth hormone treatments due to the naturally pulsatile release of the hormone in response to the agonist.

ConjuChem asserts that since human growth hormone is also the primary regulator of IGF-1, IGF-1 is the principal mediator of growth hormone release and activity in humans and animals. Furthermore, IGF-1 is a recognized surrogate marker of the activity of human growth hormone used in clinical trials. The Company's formulation, entitled CJC-1295, can be classified into three categories.

1. Life-saving and critical indications in adults of human growth hormone deficiency;

2. Pediatric growth disorders; and

3. Parameters that affect quality of life.

Clinical Development

CJC-1295 has been preclinically tested in dogs for a period of 10 days following a single subcutaneous administration. Three groups of six dogs were tested, demonstrating notably longer half-lives ranging from 126 to 140 hours. The dogs also demonstrated a significant increase in IGF-1 secretion, even at 10 days post-administration. Preliminary toxicology studies have also been conducted in rats and dogs following acute subcutaneous or IV routes of administration. CJC-1295 was well tolerated following a single subcutaneous administration. Further studies are also planned. Table 16 provides an overview of the Company's planned Phase I and IIa clinical trials. ConjuChem plans to initiate additional animal studies, combined with human studies in the second quarter 2004.

Table 16

CJC-1295: PHASE I AND PHASE IIA TRIALS

Trial	Description	Status	Comments
Phase I ascending dose in volunteers with low growth hormone levels (5 to 8 cohorts of 6 subjects).	Single dose IV and SC End points: Safety to MTD, pharmacokinetic and PD on GH and IGF-1 plasma concentrations.	To start 2Q 2004 if continued funding for the program is available in Europe and/or U.S.	Company expects product to be well tolerated. May see some nausea at high doses.
Phase I multiple dose in volunteers with low growth hormone levels (6 to 10 cohorts of 5 subjects).	Multiple dose IV and SC. End points: Safety, pharmacokinetic and PD on GH and IGF-1 plasma concentrations. Interval between two doses based on PK/PD.	To start under U.S. IND at the end of the single dose.	Key study to establish the interval between two doses.
Phase I SC re-challenge trial in 15 volunteers.	Trial designed to study the potential for immunogenicity of CJC-1295. End points: Clinical signs, measurement of antigen-speciffic IgE and IgG, and lymphocyte activation.		Previous study with CJC-1008 and CJC-1131 showed no immunigenic reactions (clinical or biological).
Phase IIa, fixed intervals with 3 dose levels versus placebo in patients with GH deficiency .4 groups of 50 to 70 patients. Duration 3 months.	End points: Safety, pharmacokinetic and efficacy on GH and IGF-1, IGF-1 binding protein; body composition, bone density; and quality of life.		

Source: ConjuChem, Inc.

Preclinical Development Programs

In addition to the two clinical stage development programs underway (pages 16-25), the Company has a number of earlier stage product development programs that are highlighted in Table 17 and further described below.

Table 17
ConjuChem, Inc
PRECLINICAL PROGRAMS

Product Program	Description	Status
DAC: NP	Long-acting ANP or BNP peptide for heart failure	Lead compound identified
DAC: Insulin	To provide basal level of insulin through long acting peptide	Lead compound identified
DAC: HIV	Long-acting peptidic entry inhibitor	Lead compound identified

Source: ConjuChem, Inc.

Congestive Heart Failure

Congestive heart failure describes any condition in which the heart is unable to adequately perform its function of pumping blood throughout the body and/or prevent blood from "backing up" into the lungs. When congestive heart failure occurs, the heart is unable to provide blood flow to other organs such as the brain, liver, and kidneys. While congestive heart failure is considered by many to be a specific disease, it can actually be considered a symptom of impairment, resulting from an underlying disease that hampers the heart's pumping function.

Many diseases can be connected to congestive heart failure, with the most common being coronary artery disease, high blood pressure, longstanding alcohol abuse, and disorders of the heart valves. In rare cases, viral infections of the heart muscle, thyroid disorders, heart arrhythmia, and other disorders can also cause congestive heart failure. Symptoms, detailed in Table 18, vary and depend on which side of the heart is failing, on the degree to which the related organ systems are affected, and on the body's ability to compensate accordingly.

Table 18
SYMPTOMS OF CONGESTIVE HEART FAILURE

Fatigue	While this is a relatively nonspecific symptom, individuals with congestive heart failure may see a decline in their ability to exercise. While patients may not be fully aware of the situation, they may subconsciously reduce their physical activities as a result.
Swelling (edema)	When the heart is unable to effectively pump blood throughout the body, fluid build-up may cause swelling in the ankles, legs, and possibly abdomen.
Shortness of breath	Fluid may also accumulate in the lungs, causing shortness of breath, particularly when an individual is exercising or lying flat. This also interferes with the patient's ability to sleep.
Nausea, abdominal pain, decreased appetite, and incontinence	Fluid accumulation in the liver and intestines may lead to these symptoms.

Source: Medicinenet.

DAC™:NP

Atrial natriuretic peptide (ANP) and beta natriuretic peptide (BNP) are both natriuretic peptides that have demonstrated the ability to reduce blood pressure activity by binding both ANP and BNP receptors in the kidneys. While these peptides have demonstrated high potential for treating congestive heart failure, their short half-lives have inhibited them from becoming reputable treatments. ConjuChem has a DAC™:NP program to develop a long-lasting anti-hypertensive agent, specifically for the treatment of congestive heart failure. The Company has tested 22 DAC™ derivatives of ANP and BNP to date, with several of them demonstrating dramatically increased half-lives in preclinical testing. *In vivo* duration of action is currently under evaluation in normal and hypertensive rats in a single dose SC study, with the measurable endpoints of weight gain, food and water consumption, urine collection and analysis, blood pressure, and necropsy.

HIV

HIV is a **retrovirus** that spreads throughout the body by invading immune cells and using their protein synthesis machinery to replicate. The immune system responds to this invasion by producing antibody and cellular immune responses capable of attacking HIV. While these and other responses are usually sufficient to temporarily arrest progress of the infection and reduce levels of the virus, the virus continues to replicate and slowly destroy the immune system by infecting and killing critical helper CD4+ T-cells. As the infection progresses and the amount of virus circulating in the body increases, the immune system's control of HIV weakens and the level of T-cells declines steadily to a fraction of its normal level. HIV infects a variety of immune system cells, particularly CD4+ T-cells. Once HIV enters the body, it binds to and invades CD4+ T-cells and the **replication** process begins. Replication is how HIV makes copies of itself and multiplies. In order to replicate, an HIV particle must write its genetic blueprint, in the form of **ribonucleic acid (RNA)**, into the genes of the host CD4+ T-cell. By doing this, the virus can reprogram the CD4+ T-cell and turn it into a virus-making machine. While there are an increasing number of therapies available for the treatment of HIV/AIDS, medical science is far from being able to conquer the virus and cure the disease. The difficulty in treating or curing HIV is that it is one of the most mutable viruses known to humanity. Scientists have classified HIV into at least 10 broad subtypes, and within these subtypes, there are countless strains.

DAC™:HIV-1

Recently, a new method for controlling HIV infection using a C34 peptide entry inhibitor has successfully been developed. The concept of entry inhibitor, to which T20, C34, and N36 analogues belong, is to act on the invasion of the cell by the virus before it starts rerouting the cell's machinery. Unfortunately, this new peptide requires twice-daily injections of very high doses (90 mg) to act and resistance is already starting to appear.

ConjuChem believes that its DAC™ technology could be a good fit with this extracellular mechanism of action and is currently exploring the possibilities of creating a synthesized version of these and other peptides that has potent antiviral activity and sustained plasma residence time. This drug would provide continuous protection against viral fusion and replication and would eliminate the need for frequent administration and high dosage rates. ConjuChem also believes that this may reduce the appearance of resistant virus strains.

This concept was tested during a research collaboration with Tibotec, a company researching antiviral activity. A study of the lead compounds yielded dramatic retention of duration and very high bioavailability, but following the acquisition of Tibotec by Johnson & Johnson, the study was put on hold. ConjuChem is now pursuing work in this field on its own.

Insulin

Insulin use was first approved by the FDA in 1939. Current treatments are derived from **recombinant** (human) technology, the first of which was approved in 1982. Insulin can be administered in several different ways. A majority of insulin treatments are administered subcutaneously. Most diabetics inject

insulin with a needle and syringe for delivery just below the surface of the skin. However, additional methods are available as well.

DAC™:Insulin

ConjuChem is developing DAC™:Insulin for use in diabetes therapy by supplying the basal level of insulin. DAC™ analogues have been synthesized. Preliminary tests in a variety of mouse and rat assays have shown solid trends of activity, with glucose control for well over six hours. Research in this area is ongoing.

Key Points to Consider

- ConjuChem's DAC™ technology has the potential to unlock the vast therapeutic potential of peptides. There are a multitude of well-known peptides with attractive therapeutic activities across many areas of medicine. The traditional problem of peptides, however, is that most have a brief duration of activity due to their short half-life in the human body.

- The Company's DAC™ technology has demonstrated an ability to overcome the limitations of peptides by transforming them into DAC™ predrugs. By conjugating *in vivo* and permanently the DAC™ to plasma albumin, an active peptide-carrier protein is formed that remains in the body in a safe and stable manner for extended periods of time.

- ConjuChem's lead development candidate, DAC™:GLP-1, is being developed to treat patients with Type 2 diabetes. DAC™:GLP-1 appears to be ideal for controlling blood glucose using several mechanisms of action. It is unique since it requires administration once every few days versus several times per day that is required by nearly all other treatments under development that use this mechanism of action.

- Although many companies have researched ways to extend the half-life of GLP-1 from two minutes to several hours, this duration of activity implies the drug would still have to be given several times per day. In contrast, ConjuChem estimates that DAC™:GLP-1 will require administration only once every few days.

- The Company announced in late October 2003 that it has commenced European enrollment in its first Phase II trial for DAC™:GLP-1, developed to treat Type 2 diabetes. North American sites are expected to open soon. This monotherapy study will have data from no less than 150 evaluable diabetic patients. The study is designed to assess the reduction of the HbA1c level after three months of treatment and determine the optimum subcutaneous dosage regimen. Results from this study are expected before the end of June 2004.

- ConjuChem announced during the third quarter 2003 the successful completion of a Phase I/II single dose trial with an IV formulation of DAC™:GLP-1. All primary endpoints were met. The study's safety, tolerability, and pharmacokinectic/pharmacodynamic parameters were consistent and similar to those reported from the subcutaneous dosing in Phase I/II trials reported on August 21, 2003.

- Current estimates are that more than US$8 billion is spent annually on anti-diabetic medications by 150 million people worldwide that suffer from Type 2 diabetes. It is forecasted that the market for diabetes medications could exceed US$20 billion by 2006.

- While DAC™:GLP-1 is currently the most advanced clinical program in ConjuChem's pipeline, multiple DAC™:peptide candidates have been generated and tested, a large number demonstrating that DAC™ chemistry works to extend the half-life of peptide drug candidates while maintaining sufficient biological activity for potential drug use.

- ConjuChem expects that the next compound to enter human clinical testing will be DAC™:GRF, developed to treat growth hormone deficient patients, such as those with short stature syndrome, AIDS, or the critically ill. Based on solid pre-clinical results, a Phase I trial is expected to start enrolment in the second quarter of calendar 2004.

- The key to the Company's future success will be to select peptide candidates for which DAC™ chemistry confers pharmacokinetic properties that are distinct from alternatives and for which clinical efficacy can be demonstrated into and through Phase III human trials.

Historical Financial Results

Tables 19, 20, and 21 provide a snapshot of ConjuChem's key historical financial statements, including its Statement of Operations, Balance Sheet, and Cash Flow Statement.

Table 19
ConjuChem, Inc.
STATEMENT OF OPERATIONS

Year ended October 31	2001	2002	2003
REVENUES			
Contract revenue	$1,147,285	$467,731	$171,281
Interest income	1,650,151	1,490,649	966,531
	2,797,436	1,958,380	1,137,812
EXPENSES			
Research and development	1,795,585	33,611,880	24,203,936
Investment tax credits	(1,320,000)	(1,132,928)	(1,191,724)
Net research and development expenses	16,475,585	32,478,952	23,012,212
General and administrative expenses	4,104,019	4,749,241	3,302,270
Amortization of capital assets	418,035	559,285	549,242
Financial charges	63,134	31,753	48,208
Foreign Exchange Gain		(92,676)	(167,539)
Accretion in carrying value of convertible senior unsecured note	—	1,864,282	2,469,247
	21,060,773	39,590,837	29,213,640
Net loss before income taxes	(18,263,337)	(37,632,457)	(28,075,828)
Provision for income taxes	—	—	17,000
Net loss	—	(37,632,457)	(28,092,828)
Deficit, beginning of year	(25,409,217)	(43,672,554)	(81,305,011)
Deficit, end of year	(43,672,554)	(81,305,011)	(109,397,839)
Basic and diluted loss per share	**($0.78)**	**($1.38)**	**($0.92)**
Weighted average number of common shares	23,497,389	27,219,593	30,410,261

Source: ConjuChem, Inc.

Table 20
ConjuChem, Inc.
BALANCE SHEET

October 31	2001	2002	2003
ASSETS			
Current			
Cash and cash equivalents	56,027	2,486,216	370,407
Short-term investments	33,902,138	32,662,857	41,527,861
Accounts receivable and other assets	1,401,747	664,391	598,415
Investment tax credits receivable	2,765,000	1,380,000	571,868
Total current assets	38,124,912	37,193,464	43,068,551
Long-term investments	5,734,710	4,364,876	3,413,857
Other assets		148,729	124,609
Capital assets	1,855,702	2,221,535	1,777,743
	45,715,324	43,928,604	48,384,760
LIABILITIES AND SHAREHOLDERS' EQUITY			
Current liabilities			
Accounts payable and accrued liabilities	3,426,677	5,974,992	3,545,350
Unearned revenue	—	156,173	—
Current portion of long-term debt	162,428	—	—
Total current liabilities	3,589,105	6,131,165	3,545,350
Long-term debt	229,990	—	—
Convertible senior unsecured note		21,751,287	24,220,534
	3,819,095	27,882,452	27,765,884
Shareholders' equity			
Capital stock	84,458,783	86,586,228	119,209,080
Equity portion of convertible senior unsecured note		10,026,761	10,026,761
Other paid-in capital	1,110,000	738,174	780,874
Deficit	(43,672,554)	(81,305,011)	(109,397,839)
Total shareholders' equity	41,896,229	16,046,152	20,618,876
	45,715,324	43,928,604	48,384,760

Source: ConjuChem, Inc.

Table 21
ConjuChem, Inc.
CASH FLOW STATEMENT

Year ended October 31	2001	2002	2003
OPERATING ACTIVITIES			
Net loss	($18,263,337)	($37,632,457)	($28,092,828)
Items not affecting cash:			
Amortization of capital assets	418,035	559,285	445,750
Amortization of deferred financing fees	—	20,850	24,120
Amortization of premium on investments	161,572	34,196	73,718
Accretion in value of convertible senior unsecured note	—	1,864,282	2,469,247
Stock options granted to a consultant	—	—	42,700
	(17,683,730)	(35,153,844)	(24,933,801)
Net changes in non-cash working capital balances relating to operations	(322,288)	4,826,844	(1,711,707)
Cash flows relating to operating activities	**(16,006,018)**	**(30,327,000)**	**(26,645,508)**
INVESTING ACTIVITIES			
Acquisition of short-term investments	(49,205,541)	(90,603,561)	(150,875,086)
Proceeds on maturities of short-term investments	15,480,050	91,808,646	141,936,364
Acquisition of capital assets	(925,737)	(925,118)	(105,450)
Acquisition of long-term investments	(3,334,383)	(3,362,419)	(3,413,857)
Proceeds on maturities of long-term investments	3,119,830	4,732,253	4,364,876
Cash flows relating to investing activities	**(34,865,781)**	**1,649,801**	**(8,093,153)**
FINANCING ACTIVITIES			
Issuance of convertible senior unsecured note		30,000,000	—
Issue costs of convertible senior unsecured notes		(255,813)	—
Repayment of long-term debt	(162,429)	(392,418)	—
Issuance of common shares for cash	57,741,295	1,780,323	34,789,502
Share issue costs paid in cash	(4,663,212)	(24,704)	(2,166,650)
Repurchase of common shares	(12)		
Cash flows relating to financing activities	**52,915,642**	**31,107,388**	**32,622,852**
Net increase in cash and cash equivalents during the year	43,843	2,430,189	(2,115,809)
Cash and cash equivalents, beginning of year	12,184	56,027	2,486,216
Cash and cash equivalents, end of year	56,027	2,486,216	370,407
Supplemental cash flow information:			
Cash paid during the year for:			
Interest	50,592	15,320	9,648

Source: ConjuChem, Inc.

Risks

Some of the information in this report relates to future events or future business and financial performance. Such statements can be only predictions and the actual events or results may differ from those discussed due to, among other things, the risks described in ConjuChem's reports in its Annual Information Filing (AIF), press releases, and other forms filed from time to time. The content of this report with respect to ConjuChem, Inc. has been compiled primarily from information available to the public and released by ConjuChem, Inc. through news releases and through Toronto Stock Exchange (TSX) filings. ConjuChem is solely responsible for the accuracy of that information. Information as to other companies has been prepared from publicly available information and has not been independently verified by ConjuChem, Inc. [Certain summaries of scientific activities and outcomes have been condensed to aid the reader in gaining a general understanding.] For more complete information about ConjuChem, refer to the Company's website at www.conjuchem.com.

Competition

The field of biotechnology is one of rapid change and innovation. ConjuChem expects that this industry will continue to experience technological changes in the years ahead. The Company operates in highly competitive markets and may experience competition from companies, which have similar or other technologies and forms of treatment for the diseases that are targeted. ConjuChem also may experience competition from companies that have acquired or may acquire technology from companies, universities, and other research institutions. As these companies develop their technologies, they may develop proprietary positions in the areas of ConjuChem's core technologies or obtain regulatory approval for alternative technologies or commercial products earlier than ConjuChem. Other companies are developing products to address the same diseases and conditions as ConjuChem and may have or develop products that are more effective than those based on the Company's technologies. Examples of some of ConjuChem's leading competitors are described below.

DAC™:GLP-1

Amylin and Eli Lilly & Company. Amylin Pharmaceuticals, collaborating with Eli Lilly & Company, is developing Exentatide, which is the most advanced GLP-1 related drugs for the treatment of Type 2 diabetes in terms of clinical testing. While this product could receive approval, it will likely require multiple daily dosings initially. Additionally, since the product is obtained from animals, there is some concern for cross-species immunogenicity. Exentatide is a first-in-class compound that has thus far demonstrated similar glucoregulatory properties to the human hormone GLP-1, but has a long lasting effect in the human body (approximately eight hours).

Amylin and Eli Lilly & Company. Amylin Pharmaceuticals and Eli Lilly & Company are in a collaboration to develop a second-generation sustained release version of Exenatide called Exenatide LAR. This compound is in early clinical development, but is likely to suffer from the same antibody generation concern as its twice-daily parent formulation.

Novo Nordisk. Novo Nordisk is developing Liraglutide (NN2211), as a stable once-daily analogue of the human GLP-1. The pharmacokinetic half-life of the compound, which is approximately 12 hours, has shown effects on the blood glucose for approximately 24 hours post-injection. This compound has recently completed a Phase II trial, with a Phase III trial initiation likely to take place by mid-2004.

Aventis and Zealand Pharma A/S. Aventis and Zealand Pharma A/S recently signed a licensing agreement for the development and worldwide commercialization of ZP10, a GLP-1 receptor agonist of the exendin class, which offers the potential to become a new Type 2 diabetes treatment. The compound is currently in Phase I/II trials using a once-daily dose.

Novartis. Novartis is developing LAF-237, an inhibitor of dipeptidyl peptidase IV (DPP-IV) for use in the treatment of Type 2 diabetes. This compound works by increasing the natural levels of GLP-1 and by blocking the DPP-IV enzyme, which metabolizes GLP-1. Recently presented Phase II results demonstrated increased GLP-1 levels and improved HBA1c after 12 weeks.

Theratechnologies. Theratechnologies Inc. is working on a ThGLP-1 molecule, which is a stabilized GLP-1 analogue for the treatment for Type 2 diabetes. Currently in preclinical development, this compound is expected to begin trials in the first half of 2004.

Human Growth Hormone

Genentech's Nutropin, Pfizer's Genotropin, Eli Lilly & Company's Humatrope, Novo Nordisk's Norditropin, and Serono's Saizem use recombinant DNA technology with the same amino acid sequence as human growth hormone produced naturally in the human body. These compounds are FDA approved for several indications, including growth failure in children due to growth hormone deficiency, short stature associated with Turner syndrome and for the replacement of endogenous growth hormone in patients with adult growth hormone deficiency.

Serono. Serono markets two other formulations of human growth hormone, both of which had been granted Orphan Drug Status in the U.S. and each being the only drug specifically approved for the treatment of AIDS wasting (Serostim in August 2003, with a 1996 accelerated approval) and **short bowel syndrome** (SBS, Zorbtive in December 2003), respectively.

Theratechnologies. Theratechnologies is developing a long-acting GRF analogue, which is currently in a Phase II trial for a number of indications, which include muscle wasting observed in chronic obstructive pulmonary disease and hip fractures, HIV-related lipodystrophy, and immune and cognitive dysfunctions.

Regulatory

The preclinical and clinical testing process to obtain FDA approval of a biological drug is costly and time consuming. As with all other products in development, ConjuChem's products will be subject to extensive FDA regulation throughout the product development process and there can be no assurance that any of the Company's products will be successful at securing the requisite FDA marketing approval on a timely basis, if at all. Clinical testing, manufacture, promotion, and sale of ConjuChem's products are subject to extensive regulation by numerous governmental authorities in the U.S., principally the FDA and corresponding state and foreign regulatory agencies. Additionally, the regulatory approval process for such products requires substantial resources and can take many years. There is always a risk that any additional regulatory approvals required for its products will not be obtained in a timely manner. ConjuChem's viability depends on its ability to produce scientific advancements and to successfully achieve the milestones as defined in its research collaborations. The Company's success will be a function of its ability to advance clinical development and obtain regulatory approval for the therapeutic products under development.

Patents and Technologies

ConjuChem currently has 30 patents that were issued or granted and an additional 170 pending patent applications. The Company believes that its diverse patent portfolio plays a key role in the overall vitality and success of its business operations. The Company employs a multi-tiered approach to building patent protection that involves patents with various broad technology claims in addition to patents with specific composition of matter, disease indication, and manufacturing process claims. ConjuChem is dedicated to filing patent applications in a variety of key markets throughout the world. There is no guarantee that the Company will obtain patents in the countries in which patent applications have been filed, or that it will develop other patentable products or processes. The failure to obtain the necessary patents for its therapeutic products could have a material adverse effect on the Company.

Additional Risks

ConjuChem is dependent on partners for the commercial development of its products. The Company does not currently have, nor does it expect to have in the near future, sufficient financial resources and personnel to develop and market its products on its own. Accordingly, the Company expects to continue to depend on larger companies for revenues from sales of products, research sponsorship, and distribution of its products.

The process of establishing partnerships is difficult and time-consuming. Discussions with potential partners may not lead to the establishment of new partnerships on favorable terms, if at all. If new partnerships are successfully established, the partnerships may never result in the successful development of product candidates or the generation of significant revenue. Management of relationships with these partners would require significant time and effort from its management team; coordination of its research with the research priorities of its corporate partners; effective allocation of resources to multiple projects; and an ability to attract and retain key management, scientific, and other personnel.

Recent Events

03/11/2004—Announced financial results for the first quarter ended January 31, 2004. Net loss for the three-month period ended January 31, 2004 was $8.3 million, or $0.20 per share compared with $6.5 million or $0.24 per share a year ago. The increase is largely the result of higher R&D expenses relating to greater levels of clinical trial activity.

02/11/2004—Provided an update on the progress of its clinical development programs at its Annual Meeting of Shareholders at the Vogue Hotel in Montreal, Canada, where the Company outlined the next series of significant milestones for its drug development programs. With respect to the DAC™:GLP-1 program, ConjuChem's Phase II monotherapy trial continues to rapidly enroll patients in both Europe and North America and remains on schedule to have main results available before the end of June 2004. Also, concerning its DAC™:GLP-1 program, the Company has decided to accelerate the start of its second Phase II trials, a combination study that will see Type 2 patients treated with both DAC™:GLP-1 and other commonly prescribed diabetic medications. The Company also confirmed that its next compound to enter human clinical testing will be DAC™:GRF, developed to treat growth hormone deficient patients, such as those with short stature syndrome, AIDS, or the critically ill. Based on very solid pre-clinical results, a Phase I trial is expected to start enrolment in the second quarter of calendar 2004.

01/12/2004—Announced financial results for the fiscal year ended October 31, 2003. ConjuChem's net loss for the twelve-month period ended October 31, 2003 was $28.1 million, or $0.92 per share, compared with $37.6 million, or $1.38 per share, a year ago. During the year, the Company was able to significantly strengthen its balance sheet by raising gross proceeds of $37 million in two separate financings. As at October 31, 2002, the balance sheet reflected cash, cash equivalents and investments totaling $45.3 million.

11/03/2003—Announced that under the terms of its bought deal financing completed on October 6, 2003, the underwriters syndicate led by Orion Securities Inc. and including Sprott Securities Inc. and BMO Nesbitt Burns Inc., has exercised, in full, its over-allotment option. Accordingly, ConjuChem has issued an additional 780,000 common shares at a price of $4.15, for gross proceeds of $3,237,000. The exercise of the over-allotment option increases total gross proceeds from the offering to approximately $24.9 million.

10/27/2003—Announced it has begun European enrolment in its first Phase II trial for DAC™:GLP-1, developed to treat Type 2 diabetes. This monotherapy study at sites in North America will generate data from no less than 150 evaluable diabetic patients. The study is designed to assess the reduction of the HbA1c level after three months of treatment and determine the optimum subcutaneous dosage regimen. Results from this study are expected before the end of June 2004.

10/27/2003—Announced the successful completion of a Phase I/II single dose trial with an IV formulation of DAC™:GLP-1. All primary endpoints were met. The study's safety, tolerability and pharmacokinectic/pharmacodynamic parameters were consistent and similar to those reported from the subcutaneous dosing in Phase I/II trials reported on August 21, 2003. The MTD was not reached as a function of the drug being well tolerated, even at the highest dose level of 12 mcg/kg.

09/16/2003—Announced financial results for the third quarter of fiscal 2003 ended July 31, 2003. The Company's net loss for the quarter was $6.7 million or $0.22 per share compared to $9.4 million or $0.34 per share for the same period last year. Net loss for the nine-month period ended July 31, 2003 was $20.0 million or $0.70 per share compared to $26.4 million or $0.97 for the same period a year ago.

08/21/2003—Announced positive clinical results from its proprietary DAC™:GLP-1 compound indicated for the treatment of Type 2 diabetes. The data came from the completion of a Phase I/II multidose clinical trial and re-challenge study to assess the compound's absence of immunogenicity. The Phase I/II primary endpoints were met: a statistically significant reduction in the average mean daily glucose level, a statistically significant reduction in the fasting glucose level, and the complete absence of adverse immune responses. The compound was well tolerated by patients at all dosing levels.

06/26/2003—Announced financial results for the second quarter of fiscal 2003, ended April 30, 2003. The Company's net loss for the quarter ended April 30, 2003 was $6.7 million or $0.24 per share compared with $10.9 million or $0.40 per share for the quarter ended April 30, 2002. The decrease in net losses is due primarily to a refocusing of R&D resources on DAC™:GLP-1 clinical trials and a consequent reduction in headcount and related expenses.

06/11/2003—Announced positive preliminary results from the four ongoing Phase I/II clinical trials for its proprietary DAC™: GLP-1 compound indicated for the treatment of Type 2 diabetes. The results indicated that DAC™:GLP-1 has the potential to effectively control glucose levels in Type 2 diabetes patients without safety concerns.

06/11/2003—Announced that, effective July 15, 2003, Jacques Lapointe will assume the position of Interim President and Chief Executive Officer. Since November 2002, Mr. Lapointe has served as Chairman of the Board and will also continue in this role.

05/08/2003—Announced receipt of clearance from the FDA to begin clinical trials in the U.S. with its proprietary DAC™:GLP-1 compound for the treatment of Type 2 diabetes.

03/19/2003—Announced initiation of the multi-dose component of its DAC™:GLP-1 Phase I/II clinical trial program.

03/18/2003—Announced financial results for the first quarter of fiscal 2003, ended January 31, 2003. The Company's net loss for the quarter was $6.5 million or $0.24 per share compared with $6.1 million or $0.23 per share one year ago. The cash burn for the period was $5.8 million or $1.9 million per month, a 34% reduction from the 2002 monthly average of $2.9 million.

02/20/2003—Announced resolution of formulation issues which had interrupted the Company's DAC™:GLP-1 clinical program. The Company resumed its single-dose Phase I/II trial on February 20, 2003 and is planning to commence a multi-dose trial later in March 2003.

12/13/2002—Announced results from the DAC & 3153: Opioid (CJC-1008) Phase II Proof of Concept trial for the prevention of pain following a hysterectomy. The results, while not statistically significant, showed efficacy trends and all time points during the patients' hospitalization period.

12/12/2002—Announced financial results for the year ended October 31, 2002. The Company's net loss for the 12-month period ended October 31, 2002 was $37.6 million or $1.38 per share compared with $18.3 million or $0.78 per share one year ago.

11/20/2002—Announced that, effective immediately, Jacques Lapointe assumes the positions of Chairman of the Board and Chairman of the Executive Committee.

10/07/2002—Announced that results from its Phase I clinical trial for DAC™:GLP-1 (CJC-1131), a compound under development for the treatment of Type 2 diabetes, are expected in the first half of 2003, as a result of the need to manufacture a reformulated clinical batch of the compound in order to complete the trial. Results initially were expected to be ready by late 2002.

9/16/2002—Announced financial results for the third quarter ended July 31, 2002. Net loss for the three months ended July 31, 2002 was $9.4 million or $0.34 per share compared with $4.9 million or $0.21 per share for the three months ended July 31, 2001.

09/05/2002—Announced that its Board of Directors had accepted the resignation tendered by Robert S. DuFrense as President and Chief Executive Officer and Director of the Company.

08/08/2002—Announced results from three clinical trials of DAC™:Opioid (CJC-1008), a peripherally acting opioid drug for the treatment of moderate to severe pain. Two of these trials were Phase II Proof of Concept trials, one in patients undergoing total knee replacement surgery and one in patients suffering from post herpetic neuralgia (PHN). A third trial was a repeat dose trial in healthy volunteers to assess the immunogenicity potential of the compound.

08/08/2002—Announced the termination of development activities for its DAC™:TI (Thrombin Inhibitor) compound.

07/08/2002—Announced the initiation of healthy volunteer dosing as part of a Phase I clinical trial for DAC™:GLP-1 (CJC-1131), a compound under development for the treatment of Type 2 diabetes.

06/07/2002—Announced financial results for the second quarter of fiscal 2002 ended April 30, 2002. Net loss for the three months ended April 30, 2002 was $10.9 million compared with $5.1 million for the three months ended April 31, 2001.

06/13/2002—Announced the presentation of four papers (one oral presentation and three posters) that describe the different ways in which the Company's DAC™:GLP-1 candidate could be used to improve upon the safety and efficacy of current methods of diabetes treatment.

06/12/2002—Announced the completion of patient enrolment for two separate DAC™:Opioid (CJC-1008) Phase II Proof of Concept trials.

05/13/2002—Announced preliminary results from a repeat dose clinical trial of DAC™:Opioid (CJC-1008) designed to evaluate the immunogenic potential of DAC™: Opioid in humans.

Glossary of Lesser-Known Terms

Albumin—The most prevalent protein in the bloodstream and key regulator of osmotic pressure. Albumin is distributed throughout virtually all tissues in the body.

Bioconjugation Process—Process of binding a DAC™ to albumin through formation of a covalent liaison with the albumin's cysteine 34 *in vivo*.

Cachexia—The loss of weight and muscle mass as a result of disease. Patients with cancer, AIDS, and other chronic diseases may become cachetic. Severity of cachexia has been linked with decreased survival in severely ill patients.

Congestive heart failure (CHF)—Any condition in which the heart is unable to adequately perform its function of pumping blood throughout the body and/or prevent blood from backing up into the lungs. CHF is not a specific disease, but rather a symptom of impairment caused by an underlying disease.

Enzyme—A protein that accelerates a specific chemical reaction without altering itself.

Glucometer—A portable machine that measures blood sugar levels by requiring the finger to be pricked, and a drop of blood to be placed on a reagent strip composed of a chemical substance known to react in a specific way. Diabetics use this glucose monitor to plan their diet, medication, and insulin treatments.

Half-life—Time needed for the plasma concentration or the amount of drug in the body to be reduced by 50%.

HbA1c—HbA1c is a test that measures the amount of glycosylated hemoglobin in your blood. The test gives a good estimate of how well diabetes is being managed over time.

Human growth hormone—A natural protein produced by the pituitary gland and transported through the blood stream to specific target cells, which are located in key growth areas in the arm and leg bones. The key functions of human growth hormone are to (1) control protein synthesis, (2) tell the body how fast to burn fat calories, and (3) develop the bone structure and muscle mass of children and adults.

Hyperglycemia—A condition marked by a build-up of glucose in the blood, resulting in high blood sugar levels. Hyperglycemia is a regular symptom of Type 2 diabetes.

Hypothalamus—A central area, located on the bottom side of the brain, which controls involuntary functions such as body temperature, hunger, thirst, and the release of hormones such as human growth hormone.

***In vivo*—**Existing inside of a living organism.

Insulin—A hormone produced in the pancreas that controls the level of the sugar, glucose, in the blood. As a result, insulin allows cells in the body to use glucose for energy. A variety of insulin-based therapies are also available to aid diabetes patients in controlling their blood sugar levels.

Intramuscular (IM)—Administered into the muscle.

Intravenous (IV)—Administered into the vein.

Lipodystrophy—A disorder of the adipose (fatty) tissue, which causes a loss of body fat. Patients with this disorder can develop diabetes, insulin resistance, a high triglyceride level, and fatty liver.

Moiety—One of two parts, which are not necessarily equal.

Natriuretic Peptides—Peptides that cause an significant amount of sodium to be excreted in the urine. Natriuretic peptides also show a unique ability to relax the vascular smooth muscle which leads to reduced blood pressure and could potentially treat heart diseases, such as congestive heart failure.

Nephropathy—A kidney disease that occurs in the small blood vessels of the kidneys when damaged. While it has no early symptoms, nephropathy has a variety of adverse affects on the body's ability to excrete waste products. It also inhibits the body to retain valuable nutrients, by flushing them away. As waste continues to build up in the bloodstream and the body is deprived of these nutrients, the possibility of kidney failure increases.

Neuropathy—Any condition that refers to the nerves' inability to function correctly. In Type 2 diabetes, raised blood pressure causes nerve cells to swell and scar, eventually losing their ability to send signals to the body. In many cases, the result is burning pain, numbness or loss of feeling in the feet and legs, sexual dysfunction, and changes in the stomach and bowel functions.

Pancreas—An organ, located behind the stomach, that produces pancreatic juices, which are enzymes that aid digestion, and insulin, which helps individuals control their blood sugar levels.

Parenteral—A drug treatment that is not administered orally, but in other means, such as subcutaneous, intramuscular, or intravenous.

Pharmacokinetics—The body's reaction to certain drugs. These include absorption, metabolism, and elimination.

Pituitary gland—A small gland located at the base of the brain that secretes hormones, which control other glands and influence growth, sexual maturation, and general metabolism.

Postprandial hyperglycemia—A rapid rise in blood glucose levels after meals.

Predrug—A DAC™ is considered a "predrug" as it precedes the real active drug which is formed once the DAC™ bioconjugates to albumin. This concept is different from the better known "prodrug" approach, in which the active drug is created *in vivo* from the prodrug through either metabolization of one of its chemical functions or by splitting.

Proglucagon—A hormone secreted from the small and large intestines. GLP-1 is derived from proglucagon.

Recombinant—Genetic material resulting from the splicing of DNA fragments.

Replication—A complex process whereby the "parent" strands of DNA in the double helix are separated and each one is copied to produce a new "daughter" strand. This process is said to be "semi-conservative" since one of each parent strand is conserved and remains intact after replication has taken place.

Retinopathy—A common result of diabetes, where the small blood vessels in the eyes become fragile or blocked, potentially damaging an individual's ability to see. This disorder has no early symptoms, sometimes going undetected for long periods of time, necessitating yearly eye examinations and frequent monitoring.

Retrovirus—HIV and other viruses that carry their genetic material in the form of RNA rather than DNA. These viruses also contain the enzyme, reverse transcriptase, which transcribes RNA into DNA. That process is the opposite of what normally occurs in animals and plants, where DNA is made into RNA, hence the prefix "retro."

Ribonucleic Acid (RNA)—A single-stranded molecule composed of chemical building blocks similar to those in DNA. RNA is the sole genetic material of retroviruses and an intermediary in making proteins in all living things.

Sepsis—A condition marked by the presence of microorganisms or their related toxins in the bloodstream or tissue. Sepsis sometimes results in growth hormone deficiency.

Short Bowel Syndrome (SBS)—This rare, serious and potentially life-threatening condition, which results in impaired absorption of nutrients, follows extensive surgical removal of portions of the small intestine as a treatment for acute or chronic disorders of the intestine.

Subcutaneous—Occurring below the surface of the skin.

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