

Executive Summary

Introduction

DiaKine Therapeutics, Inc. is a start-up biopharmaceutical company developing new, proprietary drugs for unmet medical needs in diabetes and complications related to diabetes. These drugs have the potential to restate the diabetes market by stopping the progression of diabetes and reversing damage already caused by the disease. Because of their unique immune modulating and anti-inflammatory properties, these therapies may potentially benefit people with type 1 and type 2 diabetes and represent a total available market opportunity of approximately \$13B.

The Company's lead compound, Lisofylline (LSF), has had an excellent safety profile in clinical trials to date. LSF works at the cellular level by improving the function of insulin producing islet cells and protecting them from damage and premature death caused when the body's immune system turns on itself. This autoimmune action is the cause of type 1 diabetes and Latent Autoimmune Diabetes in Adults (LADA), which combined affect approximately three million people in the U.S. About three million people with type 2 diabetes use insulin due to diminished insulin production and an increasing resistance to insulin.

Results from pre-clinical studies show that LSF improves insulin secretion and protects insulin-producing β -cells found in the pancreas from the destructive, inflammatory actions of immune agents such as cytokines; cytokines are proteins produced by special white blood cells called T-cells. LSF, when used alone or in combination with other drugs, either stabilizes or actually reverses established type 1 diabetes in animal models.

Whereas LSF has been administered intravenously in clinical studies to date, studies to determine the potential for subcutaneous administration are planned for the near future. A primary focus of DiaKine's research and development is on our next generation of orally bioavailable immune modulators which have an improved spectrum of action to LSF. Two such compounds, DT22669 and DT23552, have been identified for further development and are examples of the extensive library of analogs and new structures in our patent portfolio that await discovery for future indications.

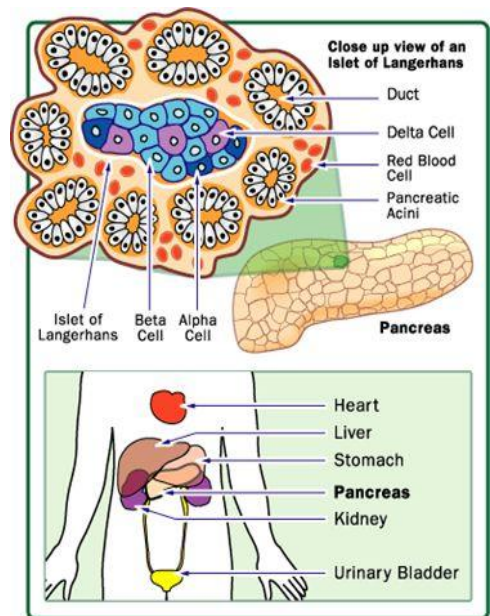


Figure 1. Close up of Islet of Langerhans

Beta cells are found situated in the Islets of Langerhans which are contained in the pancreas. The beta cells (β -cells) produce insulin. Islet cells also contain other hormone producing cells. Throughout this document and within the medical literature, islet cells and beta cells are used interchangeably.

Scientific Rationale

Diabetes

Loss of pancreatic beta cell function is the key mechanism in the development of type 1 and type 2 diabetes. Novel anti-inflammatory agents or immune modulators should prove therapeutic in diabetes and diabetic complications. Beta cell damage caused by special white blood cells called T-cells and macrophage/dendritic cells is the hallmark of type 1 diabetes and Latent Autoimmune Diabetes of Adults (LADA). Additionally, there is clear evidence that certain fats, elevated glucose, and other inflammatory cytokines can trigger progressive inflammatory damage to beta cells leading to type 2 diabetes.

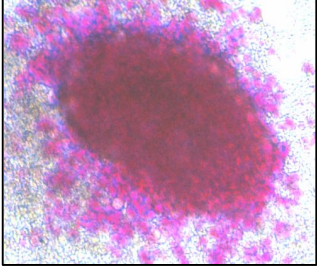


Figure 2. Human islet cell in cytokine solution being destroyed

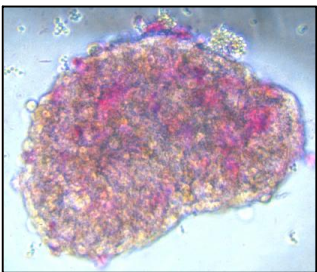


Figure 3. Human islet cell in cytokine solution protected by DiaKine drug

Diabetic Complications

Diabetes produces microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (myocardial infarction, stroke, and peripheral vascular disease) complications. Inflammatory pathways directly participate in how elevated glucose leads to these complications.

The pathogenesis of diabetic nephropathy has been clearly shown to be linked to elevated glucose and activation of the angiotensin system. DiaKine's small molecules target these key pathways of glucose and angiotensin 2 activation.

A central concept in the diabetes research community has emerged suggesting that chronic inflammation and oxidative stress plays an important role in the pathogenesis of diabetic eye disease. Inflammatory cytokines and chemokines are strikingly elevated in vitreous fluid of diabetic patients with severe forms of retinopathy. DiaKine's small molecules improve mitochondrial function and reduce the formation of the key cytokines and chemokines that lead to chronic inflammation and white blood cell adhesion in the blood vessel wall.

Market Opportunities for Products and Indications

The diabetes market opportunities for the platform technology of DiaKine's small molecules are large and growing. Segments include islet cell transplant therapy, type 1 diabetes, Latent Autoimmune Diabetes in Adults (LADA), insulin-using type 2 diabetes, and microvascular and macrovascular complications. Lead indications are:

- **As an adjunct therapy during islet cell or any other cellular transplantation engineered to reverse type 1 diabetes.**

The islet cell transplant (ICT) market represents a near to intermediate term \$20-40 M opportunity with a \$150M potential upside as technology improves. Planned uses for LSF are two-fold. First, it will

be used as a component in the islet cell culture media, thus improving the viability and function of islet cells during the procedure to isolate only the islets that contain insulin-producing β -cells from a pancreas. Second, it will be administered as a post-transplant drug therapy to keep the patient's body from destroying the new islets. If successful, islet transplantation can restore normal blood sugar without the need for insulin injections and can improve the quality of life. LSF will be one of the new drugs tested in a Phase 2 clinical trial sponsored and funded by the National Institute of Diabetes and Digestive and Kidney Diseases in the second half of 2005.

- **Reversing or arresting the progression of diabetes in type 1, LADA and insulin-using type 2 patients.**

Patients with type 1 diabetes treated with DiaKine's small molecule drugs, may be protected from further disease progression. By protecting the insulin producing β -cells, these patients may also be protected from the complications of diabetes. Preserving or restoring β -cell mass and function is a major unmet medical need for type 1 diabetes and LADA.

In addition to insulin resistance, type 2 diabetes is associated with progressive loss of the insulin producing β -cells. Therefore, use of our oral immune modulators with anti-inflammatory actions could prove therapeutic by preventing loss of the β -cells and improving glucose control.

The type 1 and LADA market represents a nominal \$1B sales opportunity assuming 150,000 patients at \$6,000 per year are treated on an ongoing basis. At the same average selling price, (ASP) a projected 25% LADA utilization rate for an oral drug with an improved spectrum of action to LSF represents approximately a \$3 B U.S. market. A utilization rate of 10% of all insulin-using type 2 patients represents a sales potential of approximately \$2 B at the same ASP.

- **Diabetes complications**

Diabetic nephropathy, or kidney disease, is one of the most frequent complications of diabetes. Up to 21% of all patients with diabetes have nephropathy. Nephropathy often ends in kidney failure or end-stage renal disease (ESRD). Approximately 43% of new cases of ESRD are a result of diabetes progression. Although certain high blood pressure medications have been found to be helpful in slowing the progression of kidney disease in diabetics, there is currently no cure.

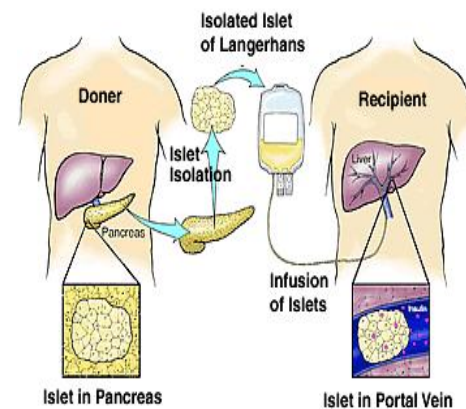


Figure 4. Islet transplantation diagram



Diabetic retinopathy leads to proliferation of blood vessels in the retina of the eye and is another frequent complication of diabetes. It represents the major cause of blindness in adults. Nearly all type 1 diabetics who have had the disease for 20 years will have evidence of diabetic retinopathy. As many as 21% of people with type 2 diabetes present with retinopathy at initial diagnosis and most eventually develop some degree of retinopathy. It is estimated that up to 24,000 people lose their sight in the United States each year due to diabetes, making it the leading cause of new cases of blindness in adults. There is no drug treatment or cure for diabetic retinopathy.

DiaKine therapy for improving islet cell transplant outcomes is scheduled to begin a National Institutes of Health-sponsored Phase 2 clinical trial later this year. We estimate that the total support from NIH to develop LSF for this indication is approximately \$1.2M.

These two complications combined cost the US Healthcare system \$48.9B in 2002. This represents an average healthcare cost of \$3.7K and \$5.5K per patient per year for retinopathy and nephropathy, respectively.

Neuropathy affects approximately 40% of all diabetics. Of the 85,000 amputations each year, 87% are due to diabetes. Type 1 and type 2 patients are equally at risk.

Cardiovascular disease due to diabetes represents an ever growing cause of mortality and morbidity. Diabetes produces up to a 14-fold risk for getting a myocardial infarction. Nearly 75% of people with diabetes die due to cardiovascular disease.

The Company has targeted the complications of diabetic nephropathy and diabetic retinopathy for development. Selection was based upon clear pre-clinical evidence supporting the efficacy of DiaKine's lead compounds in treating these two complications. Additionally, it is very possible that the compounds, by reducing mitochondrial oxidative stress, will also have efficacy in complications such as neuropathy and cardiovascular disease, as well.

Research and Development

Drug Discovery

DiaKine Therapeutics plans to continue to screen the extensive library of compounds in its platform and patent portfolio and identify candidates that demonstrate:

- oral bioavailability;
- improved potency over LSF; and
- an improved spectrum of action over LSF.







The Company will utilize highly efficient techniques to screen for new candidates and follow-up these leads using methods widely accepted by the pharmaceutical industry for drug discovery. Use of these procedures

has already identified two additional orally bioavailable compounds for further development, DT22669 and DT23552.

Drug Development and Product Pipeline

DiaKine is poised much like a development stage company because it is entering a Phase 2 clinical trial in islet cell transplantation for type 1 diabetic patients with its lead parenteral compound, LSF. Phase 1 clinical studies have been completed utilizing LSF for injection; two lead candidate compounds, DT22669 and DT23552, have demonstrated oral bioavailability in primates. One of these, DT22669, has demonstrated pre-clinical efficacy in protecting human β -cells from cytokine damage and in reducing the development of type 1 diabetes in a rodent model. DT22669 and DT23552 are also currently under development to target prevention and treatment of diabetic nephropathy and retinopathy.

Table 1. Product Development Pipeline

Product	Use	Launch			
LSF cell culture media	Pretreatment of islets	2007			
Drug products	Indication	Preclinical	Phase 1	Phase 2	Phase 3
LSF, IV	Adjunct therapy in beta cell replacement therapy or any cellular therapy engineered to reverse of diabetes				
LSF, SC	Reverse or halt progression of type 1 diabetes				
DT22669/DT23552	Treatment of insulin requiring type 2 diabetes				
DT22669/DT23552	Treatment/prevention of LADA				
DT22669	Treatment/prevention of diabetic nephropathy				
DT23552	Treatment/prevention of diabetic retinopathy				

Intellectual Property

The company holds more than 50 patents and patent applications for LSF and a wide spectrum of new structurally related and unrelated small molecules, with patents issued or pending in all major jurisdictions. The patent claims are for compositions, as well as for methods of use for various therapeutic indications with terms through as late as **2020**. Also, new patents are being developed through ongoing research and development activities.



Licensed Technology

DiaKine holds an exclusive, world-wide license to develop and market products based on the discoveries associated with LSF and the next generation of orally bioavailable immune modulators with an improved spectrum of action for the treatment of both type 1 and type 2 diabetes, metabolic syndrome, and related complications.

DT22669 and DT23552 are oral drugs we are developing to address type 2 diabetes and diabetes-related eye and kidney complications.

As part of the license agreement with Cell Therapeutics, Inc., (CTI) DiaKine has acquired the Investigational New Drug Application (IND) for LSF as well as the chemistry, manufacturing, and controls information, non-clinical pharmacology and toxicology data, and clinical trial data for use in DiaKine sponsored product development. The ownership of the technology (*i.e.* drug development and safety data) **represents a four year savings in time and development costs.**

Over 2,000 chemical variants of the LSF structure in several families have been synthesized. Two of the lead oral compounds were further analyzed for toxicity using a pharma screen and for pharmacokinetics in primates. Both demonstrated oral bioavailability and no significant toxicity in the pharma screen (Non-GLP). Thus, these two compounds are lead candidates for further development in indications of interest to the Company.

Strategy

DiaKine's strategy is to leverage its experience in the pathogenesis of diabetes and related complications to advance development of Lisofylline and its next generation of orally bioavailable immune modulators with an improved spectrum of action to LSF. Our focus is to discover and develop drugs that protect and enhance the body's insulin producing capabilities and reduce or prevent diabetes-related complications for both the type 1 and larger type 2 markets.

In support of its strategy, the Company plans to:

- Deepen its position as a preeminent diabetes company by leveraging and extending its expertise in drug discovery and development; and
- Partner with pharmaceutical and biotechnology companies, foundations, academic institutions and government organizations to accelerate product development, as well as defray costs in the form of non-dilutive financing.
- Capitalize on the licensed technology, which includes chemistry manufacturing and controls information, pre-clinical pharmacology

and toxicology data, and clinical data, to the maximum extent possible.

Competition

Every company that is marketing and/or developing products to treat diabetes and associated complications is effectively a competitor to DiaKine Therapeutics. These include multi-national pharmaceutical firms (e.g. Eli Lilly, Pfizer, Novo Nordisk, and Novartis) as well as smaller and mid-size biopharmaceutical companies. DiaKine competes on the basis of its scientific approach to treatment options, the proprietary nature of its products and the level of resident expertise associated with the Company.

The Company also competes with other pharmaceutical and biopharmaceutical firms developing immune modulating compounds. These include a variety of biopharmaceutical firms marketing and developing biological compounds having effective immune modulating characteristics. A number of multi-national pharmaceutical firms are marketing or developing synthetically derived compounds as immunosuppressive agents. Protein-based products and generalized immunosuppressive agents have a variety of limitations. DiaKine Therapeutics has a competitive advantage in that there is no apparent competition in clinical development with a synthetic small molecule to disrupt the inflammation pathway and protect β -cells.

While many these firms may be current competitors, some will also be prospects for corporate collaborations in the development of certain products that in combination may produce an enhanced therapeutic outcome. They may also become partners in the sales and marketing of the DiaKine's product candidates. The Company welcomes collaborative partnership opportunities.

Operating Plan

DiaKine currently operates with resources from the Founders, Convertible Note Participants, and government grants. The Company intends to build its operations incrementally as scientific and business milestones are achieved. Plans are in place to develop a near term (islet media) sales revenue stream which will further assist in product validation. The end game is to become a product development firm addressing the diabetes market initially and perhaps additional diseases where immune-modulation may be therapeutic in the future. DiaKine expects to collaborate with corporate partners on the initial product pipeline as clinical milestones are achieved and would expect to continue with that model in future programs. Such partners possess the potential of providing

As part of the license agreement, DiaKine acquired the IND from Cell Therapeutics, Inc. This data package represents a four year savings in time and development costs for DiaKine.



various **exit points for investors**. The longer-term view may permit the Company to market certain products to specified markets directly.

The Company has already applied for and was successful in receiving financial and technical support to produce clinical trial supplies from the National Institute of Diabetes & Digestive & Kidney Diseases/National Institutes of Health (NIDDK/NIH). **It is estimated this support under the NIH/NIDDK T1D program is valued at approximately \$250,000.** Additionally, the National Institutes of Health (NIH) is currently funding a clinical research trial entitled "Strategies to Improve Long Term Islet Graft Survival" through an Islet Transplant Consortium. The top five islet transplant centers in the world have received a \$75 M grant to advance the science of the islet cell transplant procedure. DiaKine's LSF has been chosen as one of the few, new agents to be tested clinically, starting in the second half of 2005. **This support is estimated to be valued at \$1,000,000.** It is expected that more support will be forthcoming following positive clinical results.

Over the next eighteen to twenty-four months, DiaKine will focus on several key tasks, including:

- Secure the financial resources to support its corporate development and operating plan;
- Develop LSF as culture media product for use in the preparation of islet cells for transplant;
- Produce clinical trial supplies with existing batches of LSF active ingredient;
- Conduct dose ranging studies in appropriate patient populations;
- Develop LSF as a product to treat patients undergoing islet cell transplantation;
- Bring forward a lead oral immune modulator with novel anti-inflammatory actions for chronic indications to protect the insulin producing β -cells and halt diabetes complications;
- Establish an operating team to execute scientific, regulatory and business objectives; and
- Initiate one or more corporate collaborations which are anticipated as a means of advancing the science as well as the products to the market place and a possible **exit for investors**.

Management and Directors

The Company is supported by an experienced team with demonstrated success in their respective fields. They are supported by a recognized group of research and development experts.

**KEITH D. IGNOTZ, PRESIDENT AND CHIEF EXECUTIVE OFFICER
AND DIRECTOR**

Keith Ignatz is a senior corporate executive with over 25 years of experience in the global healthcare market and 14 of those in diabetes. He joined DiaKine from SpectRx, Inc., a diabetes management company which he co-founded in 1993 and took public in 1997. Mr. Ignatz has extensive experience in venture, public, and grant financing of start-ups and development stage companies; he has raised more than \$70M in the last 10 years. Previously, he was President of Humphrey Instruments SmithKline Beckman (Japan), President of Humphrey Instruments (Germany), and Senior Vice President of Allergan Humphrey. He has a B.A. from San Jose State University and an M.B.A. from Pepperdine University. Mr. Ignatz is on the Board of Directors for Paradigm Medical Industries, a publicly traded company and AerovectRx, a privately held corporation and is a trustee of the Pennsylvania College of Optometry and Audiology.

**JERRY L. NADLER, M.D., CHAIRMAN OF THE BOARD, FOUNDER,
AND CHIEF SCIENTIFIC OFFICER**

Jerry L. Nadler, MD is Chief of Endocrinology and Metabolism at the University of Virginia and Director of the Diabetes and Hormone Center of Excellence. Dr. Nadler is recognized as a noted expert in the pathogenesis of diabetes and related complications. He has been conducting basic science and pre-clinical research on Lisofylline and oral immune modulators for the past six years under grants funded by sources including the Juvenile Diabetes Research Foundation. Dr. Nadler has been invited to sit on major advisory groups of the National Institutes of Health and the Juvenile Diabetes Research Foundation. Dr. Nadler received his M.D. degree from the University of Miami and additional specialized training at the University of Southern California. He was the Director of Diabetes and Endocrinology at the City of Hope National Medical Center prior to coming to the University of Virginia.

*Our oral compounds, **DT22669** and **DT23552**, target diabetes eye and kidney complications, which cost the U.S. healthcare system \$2 billion annually.*

**MARY ANN LATONA NADLER, FOUNDER, VICE PRESIDENT OF
REGULATORY AFFAIRS AND PRODUCT DEVELOPMENT, AND
DIRECTOR**

Mary Ann Nadler has over 20 years of pharmaceutical and medical industry experience, primarily in the area of Regulatory Affairs. Most recently, she served as a consultant to the pharmaceutical industry with a focus on small and start-up companies. Ms Nadler was Director of Regulatory and Governmental Affairs for Adenosine Therapeutics. She was employed by NeXstar Pharmaceuticals as a Regulatory Affairs Project Manager and by International Medication Systems, Ltd. as Assistant Director/Clinical Programs Manager. Ms Nadler has



successfully managed preparation and submission of INDs, NDAs, IDEs, PMAs and 510ks. Additionally, she has SBIR and STTR grant preparation and management experience with \$3.2 M awarded under her direction. Ms. Nadler holds a Bachelor of Science degree in Microbiology and is a member of the Regulatory Affairs Professional Society and the Drug Information Association.

JAMES B. FARINHOLT, JR., FOUNDER AND DIRECTOR

Mr. Farinholt has had an extensive career in the private and public sectors of finance and investment. He is a founder of Tall Oaks Capital, LP, a seed and early stage investment fund for life science, information technology and healthcare related companies. Mr. Farinholt has thirty years of experience in investment banking for small and medium-sized businesses as an executive officer at The Chase Bank in New York, in addition to Wheat First Union and Galleher & Company in Richmond, Virginia. Mr. Farinholt's public directorships are: PharmaNetics, Inc. (NASDAQ: PHAR); and Owens & Minor, Inc. (NYSE: OMI). He holds a B.S. degree from Hampden-Sydney College.

JACK W. SINGER, M.D., DIRECTOR

Dr. Singer is a founder and Director of Cell Therapeutics, Inc. (CTI). He was appointed Chief Medical Officer in January 2004 and thereby became responsible for CTI's clinical medical strategy. Prior to joining CTI, Dr. Singer was Professor of Medicine at the University of Washington and full member of the Fred Hutchinson Cancer Research Center. Between 1975 and 1992, he was Chief of Medical Oncology at the VA Medical Center in Seattle. Dr. Singer has served as an advisor to the NIH and is a consultant to pharmaceutical industry.

Financing

The Company is seeking a net \$9.5M Series A financing which is being preceded by an Onset Bridge Convertible Promissory Note Round of up to \$1.5M. The Series A financing is expected to close by the first half of 2006.