Minnesota Partnership for Biotechnology and Medical Genomics

University of Minnesota

Mayo Clinic

Business Plan

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Final Version

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Business Plan

I. Introduction

The Minnesota Partnership for Biotechnology and Medical Genomics is a unique collaborative venture among the Mayo Clinic ("Mayo"), University of Minnesota ("University"), and State of Minnesota ("State"). The Partnership[1] seeks to position Minnesota as a world leader in biotechnology and medical genomics applications that will result in important new medical discoveries, thereby improving health care for patients and supporting the development of new business and jobs in Minnesota.

In the wake of substantial breakthroughs in biological understandings and new technology, exemplified by the mapping and sequencing of the human genome, the potential for new scientific discoveries is momentous. Mayo and the University have already invested heavily in attracting important scientific talent and developing the infrastructure to support a competitive research effort. They are prepared to continue supporting this investment through a joint collaboration. However, neither Mayo nor the University can do it alone. Government investment provides the necessary leverage. The State's investment jump-starts the collaboration between the two institutions to find the areas of synergy and begin the process of translating the new knowledge into products, devices and therapeutics that also create new jobs and businesses. The State also has additional tools to facilitate this economic opportunity.

Mayo and the University recognize the potential synergy between the parties with respect to biotechnology and medical genomics research and are committed to engaging in expanded research collaborations. Researchers from both institutions have participated in discussions to develop proposed research plans, a non-confidential list of which is attached as Exhibit A. These proposals will be reviewed by panels of scientific experts to determine which projects to fund under the Partnership.

[1] While the word "partnership" is used to describe this venture, it is not meant to imply the formation of a legal partnership entity, but rather to identify the collaboration between the University, Mayo, and the State. The parties do not intend to form a legal partnership or joint venture. This document does not constitute a contract or binding agreement on the University, Mayo or the State.

The overall goals of the Partnership are to:

- Achieve breakthroughs in new methods to accurately diagnose and to develop innovative therapies for major disease areas such as cancer, heart disease and neurological disease (such as Alzheimer's), among others.
- Encourage the creation of new businesses and jobs in Minnesota that will result from these new medical discoveries.
- Maintain Minnesota as a renowned destination for medical care and the medical industry as a major contributor to the state's job base.

Specific goals are discussed in the final section of the business plan.

To achieve these goals, the Partnership anticipates requirements of $70 million over five years for programmatic needs (faculty and staff salaries, equipment, and scientific infrastructure equipment, and developmental funds to assure that technologies are effectively developed). This state money will be used to match and leverage the significant research funding already sponsored by the University and Mayo.

Scope of Activities

The scope of the Partnership is to advance medical research and discovery in disease prevention, diagnosis and therapeutics. The Partnership will fund collaborative research projects that uniquely recognize the collaborative strengths of the University and Mayo investigators. This research must advance the understanding of a disease or disease process and have a high expectation for success. This research will address issues in disease prevention, diagnosis, or therapeutics in cancer, cardiovascular disease, neurologic disease or any other area related to human health and disease. Novel applications of recent advances in biotechnology, genomics, proteomics, and bioinformatics to significant issues in human health will be emphasized. A joint committee of scientists from the two institutions will review initial research proposals. This committee will select a smaller number of proposals to be further developed into full research proposals. An External Review Panel, comprised of distinguished scientists with expertise in the areas represented by the final proposals, will recommend the awardees. In order to build on the state's initial investment, the expectation is that the investigators will seek additional outside funding (e.g., National Institutes of Health or private sector funding) to further their work. In addition, promising research that cannot be funded by the Partnership will seek alternate sources of funding.

The funding for the Partnership will be divided into two phases. Phase One of the Partnership entails funding several initial collaborative projects to develop the mechanisms for joint research (see next section for additional details). Of the $4.0 million available to the Partnership, $3.9 million is available to cover the direct and indirect research costs for Phase One, as set forth below ($100,000 will be used for incidental Partnership expenses).

Phase Two will commence when the requested $70 million is committed. The types of research to be funded, the requirements for eligible projects, and the expectations will be similar to those of Phase One projects with two enhancements. First, the experience with the Phase One projects will be incorporated into policies and procedures for Phase Two. For example, based upon the initial experience of requesting proposals from faculty who self-aggregate into research groups, we will either continue this procedure or modify it to facilitate the development of the strongest possible research proposals. Similarly, if there are therapeutic areas where collaborative proposals are not being developed, the Partnership can, at minimum, evaluate whether there are any structural impediments to research activity and act accordingly. Second, because of the longer time frame and slightly larger pool of funds for Phase Two, there will be an evaluation of more extensive, farther reaching projects that will promote the development of necessary resources to ensure the future success of the Partnership and our collective ability to implement the fields of medical genomics/proteomics and biotechnology. For example, development of additional capabilities, resources, technology and infrastructure in genomics, biomedical ethics and computer sciences may become an important part of the overall research plan. Phase Two will also permit assessment of the need for joint recruits, exchange of scientists between Mayo and the University.

Timeline

The Partnership has already undertaken Phase One, which involves substantive research projects that will demonstrate the ability of the parties to achieve scientific objectives in a cooperative and efficient manner. Using an initial investment from the state of $ 2 million matched by funds from Mayo ($1 million) and the University ($1 million), two to six collaborative research projects will be funded. Preliminary proposals (34) have been reviewed by a joint committee of Mayo and University scientists and nine have been requested to develop full proposals before December 1, 2003 (Exhibit A). These research proposals will be reviewed by a committee of distinguished scientists from outside institutions, and the awardees will be chosen and announced by February 1, 2004, at which time the two-year projects will commence.

The second phase of the Partnership will require the next round of state investment and will begin in 2005 as soon as the State has committed to investing the requested $70 million dollars (appropriations may be spread across the four or five budget years). The second phase is expected to last at least 5 years, dependent upon funding. Because state funds will serve as the catalyst to obtain additional outside funding that will provide ongoing support for established research, the duration of the Partnership should be considerably longer than the duration of the second phase of state funding and, conceivably, may exist indefinitely.

II. Financial Management of the Partnership

Statutory Funding Requirements

The University will establish designated Partnership accounts for the University-Mayo planning initiative. All funds (i.e. State, Mayo and University) will be accounted for in discrete accounts to maintain accountability. To address the statutory funding requirements, the University and Mayo will each transfer $1,000,000 of non-state funds into a designated account. Each party will identify the source of the funds being contributed as match. Half of these funds ($500,000) will be transferred by each institution approximately December 31, 2003 and the remaining $500,000 will be transferred by each institution approximately July 1, 2004.

The appropriation language states that funds shall be made available on a reimbursement basis. Implementing the Partnership's proposal under a strict interpretation of "reimbursement basis" is problematic, but the Partnership believes it can be accomplished with the following steps.

The University will prepare and maintain a consolidated reporting of the designated Partnership accounts. Disbursements will be made from the designated Partnership accounts only after review and approval of the co-chairs of the Executive Committee, or their designees. The parties anticipate that Phase I disbursements will relate entirely to funding the direct and indirect costs of research and certain incidental expenses for the Phase I research projects selected. Upon authorization, funds will be distributed to the newly established research award accounts established within the general ledger of the PI's institution.

By statute, the state makes available its matching funds of $1,000,000 in FY04 and FY05, after certification to the Commissioner. Sometime prior to February 1, 2004, and again, shortly after July 1, 2004, the University will certify the availability of non-state matching dollars in this account to the Commissioner of Finance.

When the final Phase One projects are selected on February 1, 2004, the University will submit a reimbursement request to the Department of Employment and Economic Development (DEED) for the state matching funds. This reimbursement request will include copies of the approved Phase I project budgets, and document that funds were transferred to the researcher's accounts. State funds will also be transferred to a designated Partnership account. It is expected that the first $1,000,000 from the state will be transferred shortly after February 1, 2004 and the second $1,000,000 will transferred shortly after July 1, 2004.

The Partnership would be open to changes to legislative language that provide the desired accountability, do not jeopardize the loss of funds, and provide for an efficient implementation of the projects. The Partnership will continue to work with DEED, the Department of Finance, and the Legislature to develop this language, and will present it to the 2004 Legislature.

Phase One Projects - Budgets and Accounting

Each Phase One project will include two budgets for direct project costs: a University budget and a Mayo budget. In addition, indirect costs (e.g. facilities operations and administrative costs) of research of 30% and incidental expenses (eg, costs of the external review) will be recovered by the institutions[2]. Statute prohibits project funding for direct capital costs.

The identity of the Principal Investigator (PI) will drive designation of the "institution of record" for grants management purposes. Award amounts will be distributed to institution of record for grants management purposes. The institution of record will then execute a subcontract for the other's share of grant award effort and cost.

Grant awards will be allocated in two installments. The first allocation will occur shortly after February 1, 2004 and the second and final allocation will occur shortly after July 1, 2004.

For each approved Phase One Project, the institutions will establish a unique account into which grant award amounts will be deposited. The institution of record will apply its existing administrative and financial management standards to track and report the award's financial activity.

The awards will be administered and managed as fixed price awards. However, if the principal investigator of a selected project wants to modify the original project budget, the proposed budget change will be submitted to the research oversight committee for consideration.

Access of Information and Public Accountability

Each institution will identify a point of contact for financial reporting related to the Phase One projects. These two appointed individuals will work together to coordinate timely reporting of financial data and to ensure public accountability for use of state funds in support of the projects. Financial information will be included in the interim and final reports to be delivered to the State, consistent with statutory requirements, on October 1, 2004 and July 1, 2005.

III. Inter-institutional agreements

The University and Mayo will enter into a Master Agreement and a series of sub-agreements (including an umbrella research agreement) to address their

[2] This rate for indirect costs is considerably lower than the federally negotiated rates for the University of Minnesota (48.5%) and Mayo (46%). Therefore, both institutions will be sharing with the state the costs for the research undertaken in Phase One. In addition, both institutions will be making substantial in-kind contributions (for faculty and staff time, travel expenses, etc.) in addition to their direct matches of $1 million each. The University and Mayo will not be able to contribute at this level in Phase Two and will need to have the full costs of the research program funded.

overall relationship, means of collaboration, financial management, research, the development maintenance and ownership of intellectual property, the use of facilities, visiting scientists and joint appointments, and other matters related to their relationship and the fulfillment of the goals of this endeavor. A fuller description of the parties' intent in regard to research and intellectual property is set out below. The agreements developed by the University and Mayo shall foster efficiency, timely and effective decision-making, and the appropriate stewardship of resources, while maintaining good business practices, and compliance with applicable state and federal regulations. The agreements shall be negotiated and signed no later than January 15, 2004, prior to the initiation of research projects under Phase One. Once in place, the Executive Committee or its designee will provide oversight for management of the agreements.

In general, the parties believe that the most effective model will be one in which the collaborating investigators determine a lead principal investigator at the time of submission of the research proposal. The principal investigator's institution will receive and manage the funds for the project and will subcontract with the other institution for that institution's portion of the work. The institutional policies and procedures for conducting and managing research of each institution will apply to that institution's work under each research project**.** This will incorporate the use of the well-developed systems of policy and procedure, and the trained staffs, of both the University and Mayo, and will avoid the creation of duplicative policy or administrative structures.

The umbrella research agreement to be negotiated between the parties will include standard legal terms common to such agreements and will require a specific work plan for each individual research project. Any special legal terms needed for an individual project will be included in the work plan for that project. For example, if a project will involve a scientist from one institution spending an extended period as a visitor at the other, clarification of roles and responsibilities and of intellectual property rights regarding the visiting scientist would be set out in the project work plan to the extent not addressed in the umbrella research agreement. The same would be true for any scientists hired under joint appointments to work on a funded research project. Project work plans for Phase One should be finalized by January 15, 2004, and in all cases will be in place by the start of work on February 1, 2004. Experience gained from Phase One might indicate a need to revise the master agreements for Phase Two. The agreements will provide that they may be modified by mutual written consent. Thus, not only between Phases One and Two, but also during either phase, the agreements can be readily modified to meet the needs of the Partnership.

With regard to data access and confidentiality policies, the parties will follow applicable law and regulations, and standard industry business practices. The parties shall create a conflict resolution process by which they may promptly and effectively resolve any disagreements. Conflicts that arise will be resolved, if possible, by an informal process of consultation by program directors from each party, and, if that is not successful, by the senior managers of each institution. If informal resolution is not successful, a process for expedited dispute resolution, including procedures for minimizing costs, will be utilized. The informal and

formal procedures will be set out in the Master Agreement. Any costs related to dispute resolution will not paid for out of the appropriated funds.

Commercialization of New Discoveries

Intellectual property developed under the collaboration shall be managed by common (accepted) practices among academic and non-profit entities. Ownership of inventions will be dictated by inventorship, which is a matter of U.S. patent law. The parties understand the need to effectively manage intellectual property arising out of the collaboration. This management will reduce legal costs and maximize the scope of protection obtained for new inventions. Accordingly, the institutions will develop an efficient procedure for evaluating any intellectual property arising out of the collaboration, including a process for quickly determining inventorship on patent applications. This procedure and related terms will be set forth in the umbrella research agreement as that agreement may be modified or supplemented by the terms of a specific work plan. The lead institution for commercialization of intellectual property arising out of a work plan will be selected by mutual agreement of the respective technology transfer offices. This decision will be based on where the science is taking place (i.e. where PI resides), the number of inventors and other factors. Should the parties not be able to agree on who will take the lead in managing the invention, the choice of lead institution will be decided by mutual agreement of a committee composed of a senior representative from each institution.

Internal Development of Early-stage Innovations

The preferred route for commercialization will be to license new technology to a new or existing company as soon as practical. However, new technology often requires additional investments in applied research and development before it has sufficient value to be an attractive license. For example, a new therapeutic agent might require preclinical testing (testing in an animal model of disease) or toxicological evaluation before it could be commercialized. The National Institutes of Health and foundations do not regularly fund this type of developmental work. Therefore, to prevent promising, but unproven, technology from languishing or never being commercially developed, the Partnership intends to apply approximately 5-10% of the Phase Two funds to this purpose. These development funds will not be used in lieu of outside investment of the technology, but only in instances where outside investment is premature.

Keeping the New Technology in Minnesota

A major goal for the Partnership is to contribute to the economic development of the biosciences industry in Minnesota. Both the University and Mayo are committed to licensing all new technology to qualified Minnesota-based, new or existing companies whenever feasible and consistent with applicable state and federal regulations. Additional initiatives by the state, such as using State Board of Investment funds for seed capital, will contribute to the successful economic development of the biotechnology industry and take greatest advantage of the technology developed by the Partnership.

Joint Technology Advisory Group

An advisory committee will be established to serve as an external resource for the Partnership on technology commercialization issues. The committee will provide feedback, advice and assistance in identifying an optimum commercialization route for technologies developed under the Partnership. Technologies to be brought before the committee shall be identified by the lead technology transfer office. The committee is strictly advisory in nature and shall be composed of experts from the community.

IV. Additional Participants

It is possible that as this effort progresses there will be appropriate roles and opportunities for interested Minnesota companies to be involved. The University and Mayo will continuously explore possible relationships with the private sector in regard to technology transfer or other aspects of the collaboration, which could involve the private sector in an appropriate and mutually beneficial way. Minnesota companies could be directly involved in research projects, where appropriate, or participate in technology development.

The Partnership hopes to attract investment from the federal government. Federal investment could take the form of a federal appropriation to support the ongoing infrastructure costs of the Partnership. Federal investment could also take the form of direct research grant support through agencies such as the NIH, NSF or NCI. In either case, federal funding would be administered as sponsored funding through the sponsored projects administration office of the recipient institution or designated Principle Investigator, subject to normal policies and procedures.

V. Demonstration of Incremental Value of the Partnership

Before Feb. 1, 2004, a detailed economic analysis will be conducted to quantify the economic impact of the Partnership. The detailed analysis will

summarize the extent and nature of state initiatives, including data on the outcomes of state/provider partnerships; summarize the short-term benefits of the Partnership (specifically, the ability to retain and attract key scientific talent, the potential of attracting NIH, private donor and foundation research funds, and the economic value of the leveraged research effort -- direct and indirect employment and governmental tax revenue); and determine the value of new business formations and savings to the health care industry, including the long-term benefits of patents, companies created, new jobs and additional tax base. The cost of this study will be funded by the parties. In addition, as part of the process of applying for funding, every research project will identify its potential economic value, its potential market, and potential timeline for development.

Exhibit A. Minnesota Partnership for Biotechnology and Medical Genomics

Initial Letters of Intent (applications shown in **boldface** have been selected as finalists)

Grant ID	Grant Title	U of M Investigator(s)	Mayo Investigator(s)	2 Year Budget
1	Identification of Novel Biomarkers in Diabetic Nephropathy of Type 1 Diabetes Mellitus	1	3	$600,000
2	**Small Molecules that Disrupt BAFF Complexation: New Techniques for Developing Individualized Drugs in the Post-Genomic Era**	**2**	**2**	**$500,000**
3	Comprehensive Peripheral Blood Profiling Studies: Application to Normal Aging, Cancer, Neurodevelopment, and Cardiovascular Disease	6	6	$800,000
4	Actin Isoform Proteomics in Healthy and Diseased Hearts	1	2	$311,252
5	**Endothelial Genomics and Phenotype in Early Atherosclerosis**	**2**	**5**	**$1 million**
6	**The Genetic Basis of the Hyperinflammatory Response and Atherosclerosis**	**5**	**5**	**$1,009,054**
7	**Synthesis and Testing of Smac Peptidomimetrics as Potential Chemosensitizing Agents for Breast Cancer**	**1**	**2**	**$500,000**
8	Determination of the Molecular Structure of Protein: Protein and Lipid: Protein Interactions Required for Assembly and Secretion of Apolipoprotein B Containing Lipoproteins	1	1	$500,000
9	Diagnostic Stethoscope Collaboration	2	1	$538,520
10	Gene Knockdown in Primary Mouse T Lymphocytes by Adenoviral Delivery of Small Interfering RNA Molecules	2	1	$500,000
11	Development of Dendritic Cell Vaccines for EGFRvIII Expressing Brain Tumors	2	1	$500,000
12	Cellular Therapy for Myocardial Repair: Using High-Field NMR and Micro-CT to Evaluate Cellular Trafficking, Angiogenesis and LV Function	1	1	$300,000

13	Cardiovascular Flows: Imaging, Analysis, Cellular Response, and Clinical Consequences	4	5	$900,000
14	Targeting Tumor Angiogenesis in the Treatment of Neoplastic Liver Disease	3	6	$500,000
15	**Coordinated Multi Program Utilization of Microarray Data to Generate and Validate Biomarkers for Improved Care of Patients with Prostate Cancer**	**7**	**11**	**$1,000,000**
16	Comparative Pathology of Canine and Human Atopic Dermatitis	2	2	$221,000
17	The Genomics and Proteomics of Chronic Pain through the Minnesota Pain Alliance	16	3	~$1,000,000
18	Co-reference Resolution for Text Mining from Biomedical Texts	5	5	$250,000
19	Novel Chemistry and Instrumentation for Automated, High-Throughput Drug Discovery for Neurodegenerative Disease	5	4	$1,000,000
20	Duluth-Minneapolis-Rochester Consortium to Develop an Integrated System for Clinically-Based Analysis of Proteomic and Gene Expression Data	4	2	$1,000,000
21	A Microarray Analysis of Changes in Gene Expression Associated with Antibody Mediated Vascular Damage	4	4	$250,000
22	The Mayo/U of M Coordinated Minnesota Ovarian Cancer Collaboration	4	2	$500,00
23	Development of Dominant Negative HIV VPR Inhibitors	1	1	$230,000
24	**Proteomic Design of Peptide-Based Probes for the Molecular Imaging of Amyloid Plaques to Diagnose Alzheimer's Disease Using Contrast-Enhancement Magnetic Resonance at High Field Strength (9.4T)**	**2**	**3**	**$488,538**
25	Treatment of Neurosensory Retinal Degenerations with Bile Acid	3	2	$500,000
26	**Peripheral Blood Cell Microarrays and Pathway Discovery in Rheumatic Diseases**	**5**	**6**	**$750,000**
27	**Novel Melanoma Immunotherapy Clinical Trials and Biomarkers**	**6**	**4**	**$1,000,000**

28	Targeting the Origin of Tumor Cell Heterogeneity	3	3	$500,000
29	Pharmacogenomic Clinical Trials for Severe Mental Illness (title not specifically stated in LOI)	3	3	$800,000
30	The Genomic Signature for Cancer Aggressiveness	8	12	$600,000
31	Minnesota Initiative in Xenotransplantation (MIX): I. Genetic Engineering of Source Pigs for Islet Xenografts in Diabetes	3	3	$1,000,000
32	University of Minnesota-Mayo Clinic-IBM Network (UMIN) for Pattern Discovery	9	6	$941,128
33	**Non-Volitional Activity in Obesity Resistance: Role of the Brain**	**3**	**2**	**$600,000**
34	Chemotherapy-Induced Peripheral Neuropathy and Pain Syndrome Program	1	2	$700,000
TOTAL	**Thirty-four research proposals**	**128 investigators from 12 colleges**	**121 investigators**	**$21,789,492**