DEVELOPING PITTSBURGH'S BIOTECHNOLOGY ASSETS

A Strategy for Growth

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I. INTRODUCTION

PURPOSE OF THE REPORT

The Urban Redevelopment Authority of Pittsburgh (URA) and the Western Pennsylvania Advanced Technology Council (WPATC) engaged Shorebank Advisory Services in collaboration with Arthur Young & Co. and J. Kay Noel & Associates to study the state of Biotechnology in Pittsburgh, to determine the potential for commercial application of existing research activities, and to design a strategy of intervention for this sector to accelerate its growth.

The public-private partnership espoused by the WPATC and URA and their missions of promoting new industry development and economic diversification, have prompted a closer look at the field of biotechnology in Pittsburgh. This report outlines the state of that industry, as well as recommendations designed to lead to increases in: corporate-sponsored research, licensing activity of Pittsburgh area innovations, and the formation rate of new Pittsburgh-based biotechnology companies.

For purposes of this report the term "biotechnology" is used to cover a broad spectrum of efforts. In this broader definition, we include biomedical and bioengineering technology, as well as the areas more commonly associated with the biotechnology field, such as plant and animal genetics. In this context, the University of Pittsburgh's Center for Biotechnology and Bioengineering has a useful definition: "Biotechnology is the search for the useful application of scientific and technical knowledge to solve problems associated with the biological and chemical processes of living things."

The importance of biotechnology research to Pittsburgh's academic community, as well as to the region as a whole, is substantial. Research activity in biotechnology and related fields among the area's major research institutions amounts to an estimated $100 million per year. This report concludes that long-term return on this economic activity can be advanced through a strategy which engenders centers of excellence in the scientific areas in which Pittsburgh has an edge, provides appropriate targeted supports for commercialization and technology transfer, and creates a critical mass of biotechnology activity attractive to leading researchers, entrepreneurs, and venture capitalists.

The Center for Biotechnology and Bioengineering to be located at the Pittsburgh Technology Center represents a strong public-private commitment toward the development of biotechnology research and entrepreneurial activities in the Pittsburgh area. Similarly, the recently initiated Pittsburgh Biomedical Development Corporation is designed to provide key expertise and resource support in the development of new biotechnology ventures. These two efforts in tandem with Pittsburgh's major research institutions can be important forces in sparking the growth and further development of Pittsburgh's biotechnology sector.

GOALS AND SCOPE

This report aims to generate useful discussion on the direction of public and private investment in Pittsburgh's emerging biotechnology industry. Furthermore, it provides a suggested framework for growing the industry on the local level. The challenge at hand is to take those niches in the biotechnology arena in which Pittsburgh is particularly capable and launch an integrated strategy which fosters a new level of development and interchange among: basic researchers, commercially minded corporate research sponsors, entrepreneurially minded scientists, seed and venture capitalists, and entrepreneurs themselves.

The scope of the research project brought together three areas of particular relevance: economic development policy and strategy, venture development, and technical expertise in the biotechnology field. The following tasks were undertaken in accomplishing this study:

- Interviews were conducted with policymakers (department heads and academic deans of Pittsburgh's universities and hospitals) and research directors to:

  —Ascertain from among the current array of research activities those which have the most promise for commercialization.

  —Review the common strengths of these research activities as well as their needs, opportunities, and constraints.

  —Survey the existing local efforts and support mechanisms for biotechnology with an emphasis on gaining views and insights on commercialization practices.

- Appropriate panels and focus groups composed of venture capitalists, technical specialists, biotechnology entrepreneurs and researchers were convened in order to:

  —better understand the specific steps and supporting resources necessary to commercialize particular biotechnology innovations;

  —gauge the level of interest of the venture capital network in Pittsburgh's biotechnology;

  —better understand the commercialization efforts of specific researchers and their view of the constraints they operate within.

- A list of recommendations and suggested actions was prepared which together would provide a cohesive and well-linked series of incentives and support mechanisms to stimulate local growth of the target industry.

Over 100 people in the biotechnology arena were interviewed by the project team. Those interviewed included university and research institution policymakers, researchers, entrepreneurs, and staffs of various supporting organizations. As a result of the interviews 73 biotechnology or biomedical related research projects were identified and their commercial prospects reviewed.

An advisory panel drawn from the venture capital, university, hospital and biotechnology industry communities was convened. This panel reviewed 22 biotechnology projects in a full day session. The commercialization potential was a primary factor in selecting the 22 projects out of the 73 initially considered.

Four focus groups were held in May of this year. Participants represented a cross-section of researchers and policymakers involved in areas such as non-invasive imaging, molecular biology, fluorescent markers, biosensors, cancer therapy, and biomedical devices.

Through these activities the project team made its best efforts to identify the most promising areas of research for commercialization, although the considerable level of research activity in Pittsburgh makes it unlikely that all such promising research was ferreted out by the project team and focus groups. Consequently, it is possible that some activities with high commercial potential were overlooked in this process. Nonetheless, the broad range of projects considered by the project team is a substantial sample of the research under way in the local biotechnology arena and

includes an appropriate cross-section of efforts from which to draw findings and recommendations.

Pittsburgh's strengths and limitations in the field were delineated as an outcome of these interviews and focus groups. The major criteria used in establishing Pittsburgh's strengths for purposes of this report were:

1. Do the specific efforts represent a sufficient critical mass of research activity which is focused on a central scientific problem and thereby able to make significant progress on solving that problem? How well known are the scientists and their efforts in their particular field?

2. Does the outcome of the research have foreseeable commercial potential?

3. Does the research have proprietary potential and is it likely to qualify for protection by way of patent or copyright?

By applying the above criteria, certain efforts which do indeed represent excellent science (but with somewhat less commercial potential), would not, however, be viewed as particular strengths in Pittsburgh's endeavor to create a vibrant biotechnology industry.

Likewise, excellent scientific efforts which do not have a critical mass of researchers focused on enough aspects of a particular scientific problem would not rank as highly among Pittsburgh's biotechnology industry strengths.

II. PRIMARY FINDINGS

1. Pittsburgh has Major Strengths in Biotechnology Research upon which Commercial Activities Can be Built

(a) Pittsburgh's major strengths in biotechnology research with commercial potential are:

- Medical imaging, specifically in the area of Nuclear Magnetic Resonance (NMR) technology. NMR is a non-invasive imaging technique which allows researchers and physicians to visualize the body's internal structures better than other technologies such as x-ray and CT-Scan.

  Research in this area is being conducted at the Pittsburgh NMR Center and the Pittsburgh NMR Institute and also includes the efforts to develop the LIMET (Less Invasive More Efficient Technology) Institute, by Dr. Gerald Wolf. (Dr. Wolf is also director of the Pittsburgh NMR Institute).

  By using NMR, Pittsburgh researchers are developing new methods of: determining organ viability prior to transplant, detecting very small tumors early in their development, and diagnosing neurophysiological disorders such as Alzheimer's disease, schizophrenia and manic depression. The methods and agents used in this effort should be licensable to commercial concerns provided that proprietary protection can be obtained. Commercialization of these activities could proceed either through selective licensing of the innovations emerging from the Institute or through one or more start-up ventures.

  The NMR Institute represents a strong inter-institutional effort involving the University of Pittsburgh, Carnegie Mellon University, six University Health Center hospitals and six other hospitals. The NMR Institute is involved in both clinical practice and in research. The Pittsburgh NMR Center is a joint effort of Carnegie Mellon University and The University of Pittsburgh and is involved currently in the research area only.

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- Cancer therapy research, particularly in the area of cancer immunotherapeutics. At the Pittsburgh Cancer Institute (PCI), which is working in cooperation with the NMR Institute, University of Pittsburgh and Carnegie Mellon University, biological response modifiers[1] are being developed to help the body's immune system fight cancer. Natural cells (NK and A-LAK) which kill or retard the growth of tumors are being investigated. In addition to these agents, methods are being developed to transport these and other biological response modifiers to the site of the malignancy. Both these immunological agents themselves and the methods of transport are likely candidates for proprietary protection. Both of these activities appear to have substantial licensing potential to commercial interests and may also form the basis for start-up ventures. PCI represents a critical mass of research activity with over 100 full-time staff and the involvement of over 200 researchers and physicians. PCI is the focal point for trials on biological response modifiers to be performed by the Eastern Cooperative Oncology Group of the National Cancer Institute.

(b) Other areas in which a smaller mass of research activity exists, but where a number of notable efforts are under way include:

- Biomedical data management networks, workstations, and devices. A number of investigators from Pittsburgh institutions (University of Pittsburgh and Presbyterian-University, Montefiore and Children's Hospitals) have targeted data management network and workstation projects with a range of applications.

  The work of Dr. David Gur of the Department of Radiology of the University of Pittsburgh is particularly noteworthy in this area. Dr. Gur's efforts in interfacing computer capability with radiology technology has received considerable support via corporate sponsored research funding by General Electric, IBM and others. Dr. Gur's computer work in x-ray technology has led to advances which now permit physicians and researchers to view x-rays in "real time." Gur's work entails handling and imaging enormous amounts of data from different sources. The lessons gained from developing this technology may be applicable to other researchers in this area. Dr. Gur's research group has also developed technology which can integrate data from 256

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1 Biological response modifiers are cells (such as NK and LAK cells) and molecules (such as interferons and lymphokines) which are involved in and can influence the reactions of the body's immune system.

different health care analytical devices (blood tests, urine tests and so forth).

Other projects in this area include efforts to utilize data from NMR and CT-Scan imaging techniques to visualize how and at what rates medications reach their target area (Dr. Dade Lungsford-Presbyterian-University Hospital). This technique can be useful in determining dosages and in visualizing the effects from those dosages. Another innovation involves computer processing of electrical signals emanating from nerves which will allow researchers and surgeons to diagnose the presence or lack of nerve activity in a given area as a guide to surgical procedures (Dr. Robert Sclabassi-Children's Hospital). A third researcher is developing a lab test control databank which has the potential to integrate a wide range of data and analytical tools into a central control system (Dr. Sidney Wolfson-Montefiore Hospital).

These efforts have in common the collection and sorting of data from a range of sources with an application to health care. Integrating data from NMR and CT-Scan imaging techniques; separating out electrical signals from nerve and non-nerve sources; and integrating data from a number of sources for a complete lab test control system are representative of the problems yet to be fully solved for these researchers.

The biomedical data management network and devices area is one in which the potential for new collaborations is substantial.

- Molecular Biology

  Pittsburgh's capabilities in molecular biology have grown rapidly over the last several years. Notable basic research with the long-term potential to assist other local work in cancer therapy is under way. Two projects, both within the University of Pittsburgh's Department of Biological Sciences, which have substantial potential for outlicensing to a broad range of biotechnology firms are described below:

  —Dr. Terry VanDyke's work in which ways are being found to reliably develop specific malignant tumors in mice by inserting appropriate genes and other agents at the embryonic stage. Through this approach tumors are generated spontaneously in the laboratory animal rather than via the typical method of directly inserting cancerous tissue at a later stage of the animal's development. This technique allows researchers to study tumor

development in a far more natural setting than the current methods permit.

—Dr. Jude Samulski's work to develop a mechanism by which any gene can be inserted into any type of cell. Previously, gene-specific or cell specific methods of insertion had to be developed for particular combinations of genes and cells. This innovation will greatly improve the efficiency of those researchers working on recombinant DNA technology.

- Biosensors

  Biosensors, simply put, utilize chemical, biological and/or electrical reactions to determine the presence or lack of a substance. Biosensors offer potentially more sensitive diagnostic tools in areas such as detection of toxic waste, environmental monitoring and in medicine. Researchers at the University of Pittsburgh and Carnegie Mellon University are working on a variety of projects in the area including development of a glucose sensor device (Dr. Wolfson-Montefiore Hospital). A corporate leader in this arena is Westinghouse which has invested heavily in biosensor technology over the last several years. Biosensor researchers in Pittsburgh should seek out any number of avenues of collaboration with Westinghouse in order to buttress their efforts with Westinghouse's broader commercial focus.

- Fluorescent Markers

  At Carnegie Mellon University (in collaboration with Mellon Institute and Allegheny-Singer Research Institute), Dr. Allan Waggoner and Dr. Lance Taylor have been developing distinct methods of recognizing molecules and cells for use in areas such as blood analysis. By way of example, one possible application for these markers could be in recognizing the various types of cells present in a leukemia patient's blood and could assist diagnosis and therapy by being able to ascertain the type of leukemia and state of advance of the disease. Their work has become widely known and licensing opportunities are emerging with companies that specialize in packaging complete systems for the appropriate tests for which the markers are useful. In fact, licensing discussions have been held with at least one company. Recent efforts of this research group (the Center for Fluorescence Studies) to obtain a major National Institutes of Health grant (approximately $10 million) should be vigorously supported. That level of resources dedicated to this group would dramatically expand its potential.

- Medical Instrumentation and Devices
  A wide range of independent efforts are under way in this area that includes efforts to develop an artificial kidney, a device to detect aneurysms (a pre-stroke condition) at a very early stage and a mini-implantable ventricular assist device. Although this area has numerous projects under way, there is no focus on a particular range or type of instruments or devices. By way of example, the University of Colorado's and University of Utah's efforts in artificial hearts are supported by numerous labs. The independent efforts of Pittsburgh researchers are focused on a wide diversity of devices with an equal diversity of applications.

(c) Pittsburgh's biotechnology resources also contain two support capabilities which could potentially be harnessed to encourage rational drug design research activities. Simply put, rational drug design involves the design of drugs based on the ability to predict how molecules will respond to certain agents including drugs. That predictive ability can help researchers more quickly ascertain which agents are likely to influence the molecule in a way that helps reduce the spread of disease or speed its cure.

- X-ray Crystallography. Knowing the three dimensional structure of molecules is a first step in the rational drug design process. This is accomplished through x-ray crystallography and Pittsburgh may have the largest concentration of x-ray crystallographers in the United States.

- Pittsburgh Supercomputing Center. An advanced approach to rational drug design uses a technology known as computer-aided molecular design. This technology requires development of highly sophisticated software programs which can take the structural information provided by the x-ray crystallographers and create graphic portrayals of molecular structure and modifications to those structures. It is in this connection that the Pittsburgh Supercomputing Center is a potential resource in combination with the x-ray crystallography talents. In addition to x-ray crystallography and supercomputing abilities, strong capabilities in quantum chemistry and physics would also be needed to develop a serious effort in computer-aided molecular design.

(d) Another significant strength is the clinical base of Pittsburgh's health care complex and renowned clinical practices in transplants, cardiology, oncology, neurosurgery and other areas. Corporate sponsored research for clinical trials of new medical devices and methods is growing at Pittsburgh's hospitals. The benefits to the research institutions and

hospitals are additional funding, more efficient use of the facility and a means of breaking new ground and enhancing the reputation of their clinical practices. The benefit to Pittsburgh is income from outside the region, growth of the clinical practices, stronger health care institutions and additional employment. Although this contribution to Pittsburgh's economy is significant, in terms of commercial potential for new ventures or licensing opportunities (the two primary methods of commercialization), this clinical base is not likely to generate substantial activity.

2. Pittsburgh Has a Strong Biotechnology Research Base but Must Focus its Resources Collaboratively

Pittsburgh's research base and scientific reputation provide a foundation for growing a strong biotechnology industry in Pittsburgh. There are specific areas or niches in biotechnology in which Pittsburgh has an edge and other areas which clearly could be further developed. Making the most of Pittsburgh's research strengths is constrained, in part, by the following factors:

- With two notable exceptions (in the areas of cancer therapy and medical imaging using the nuclear magnetic resonance [NMR] technique), most of Pittsburgh's biotechnology-related research is being conducted in 1-4 person research teams which are often working on only one aspect of a major scientific problem. The inherent difficulty in this approach is that it is harder to make significant progress on complex scientific problems. And without significant scientific progress it becomes harder to attract the necessary research dollars to mount such an effort. These factors contribute to a lack of critical mass of talent and resources focused on solving specific scientific problems with commercial potential.

- Institutional arrangements need to be fostered which promote and facilitate collaboration between researchers working on related problems in different departments within the same research institution and researchers from among different institutions. Opportunities appear to exist to focus a variety of research talent from various institutions and departments on central research problems.

Ease of collaboration between researchers from the major research institutions (University of Pittsburgh, Carnegie Mellon University and Allegheny-Singer Research Institute) is essential for gaining a critical mass of activity in

biotechnology. Without focusing resources and organizing talents on select areas of science with commercial prospects, the economic potential of Pittsburgh's capabilities in this area will not be fully realized.

3. Common Factors Act as Constraints to Commercialization of Existing Biotechnology Research

During the course of the project team's survey of existing biotechnology efforts, 73 projects at varying levels of development and commercial potential were identified. The 73 projects reviewed involved a wide range of innovations, processes and devices. The largest concentrations of activity discovered were in: medical devices (32%); therapeutic (19%) and diagnostic (10%) agents or treatments.

Nearly all of the projects were found to be at an early stage of development with commercialization anywhere from 3 to 7 years distant.

The projects and their researchers/developers are confronted with a series of constraints:

- Lack of access to or specialized knowledge of the potential markets for their innovation, the competition they face, and which corporations may be interested in their technologies.

- Lack of access to patent counsel with specific knowledge of biotechnology and the ability to assess quickly the proprietary position of innovations. (The commercial potential of any innovation is directly related to its proprietary position and protection. Without such protection the researcher and his or her institution can find themselves in a less attractive position on either corporate licensing of the innovation or in discussing its value with seed or venture capitalists in a start-up company scenario.) Researchers at institutions, such as Stanford, are able to obtain proprietary protection in a matter of weeks with the availability of specialized counsel. This is in sharp contrast to the experience of most Pittsburgh investigators seeking patents or copyrights on their work.

- Lack of knowledge of, access to, and representation with major corporations interested in providing sponsored research dollars or obtaining the licensing of biotechnology research and innovations. Many researchers are unfamiliar with those corporations which may have an interest in their work and how to approach them. And when the attention of major corporate sponsored research or licensing staff is obtained, in many instances little guidance is provided to the researcher in negotiating terms of those agreements. Researchers are understandably hungry for research dollars and the immediate need for research funding often overshadows the prospect of negotiating more limited rights to the research for the sponsoring corporation.

Much of the knowledge and guidance needed by the researchers is industry specific to biotechnology. Generalized efforts at commercialization and technology transfer are not likely to be very helpful due to the nature of the industry and its specialized markets, technology and network of contacts.

4. <u>Pittsburgh has a Limited Infrastructure for Biotechnology Venture Start-ups</u>

Presently there are a dozen or more Pittsburgh area companies which would be characterized as small or medium-sized biotechnology firms. These firms employ an estimated 800 people. This is a small but important base upon which to build further. By comparison, biotechnology hot spots such as Palo Alto and Boston have spawned hundreds of biotechnology firms. This lop-sided comparison can change over time as the existing firms prosper and create spin-off opportunities and as the critical mass of research and commercialization activities builds.

In order to accelerate the formation rate of biotechnology firms in the Pittsburgh area, additional venture development support functions and talents are needed. In particular:

- Commercial development grants and pre-seed capital funding are needed to move existing research projects to a more conventionally "investable" stage.

- Well-packaged promotion of emerging Pittsburgh innovations is needed to the network of biotechnology industry entrepreneurs, technical specialists, seed and venture capitalists, licensing staffs of major corporate actors in the industry, and industry trade journals.

- The top and middle management recruitment function Pittsburgh has developed in other high technology areas (such as exists for software firms) needs to be replicated for biotechnology.

Resources to fund research projects to a more investable stage, attract and develop the specialized talents and experience necessary to support commercialization efforts, and attract the attention of venture capitalists, entrepreneurs and major corporations to Pittsburgh's biotechnology potential are each critical elements of the necessary infrastructure for fostering biotechnology venture start-ups.

5. A Culture which Encourages Commercial Development is Needed

Pittsburgh's climate for development of a biotechnology industry is improving. The development of the Pittsburgh Technology Center and the Center for Biotechnology and Bioengineering are essential ingredients in that improvement. The recently initiated Pittsburgh Biomedical Development Corporation will also provide specific resources and talents to focus existing Pittsburgh capabilities on commercial avenues of pursuit.

Universities, and to a lesser degree medical research facilities, are by definition not commercial ventures in the classic sense. The culture of these institutions rewards scholarship, science and practice—not commercial potential. Pittsburgh's institutions are no different in this regard. Researchers, too, are often more inclined toward pure scientific advance than commercial potential, and many observers of academia and science say that this is proper and as it should be.

The entrepreneurial climates of Palo Alto and Boston have overcome these biases and learned to work within their constraints. Encouragement of a new mindset towards commercial opportunities in the biotechnology arena is very much needed if a biotechnology industry is to emerge in Pittsburgh. More emphasis on seeking out commercial avenues for existing efforts is essential at academic and research institutions, organizations which support commercialization efforts, and among researchers themselves.

The natural constraints of academic institutions in regards to commercial endeavors suggest that many of the support mechanisms for improving the emphasis on opportunities should be housed within organizations which are semi-autonomous, community-wide resources rather than research institution-specific organizations.

III. RECOMMENDED STRATEGY

ISSUES

Developing Pittsburgh's biotechnology industry will require a generation-long commitment of energies and resources. It should be noted in a similar light that Pittsburgh's capacity in computers and software was developed over such a generational timespan. The computer area is seeing the results of that effort today in increased research dollars, new venture formation and venture capital and corporate interest. The institutional will to sustain the effort to develop Pittsburgh's biotechnology industry over a 15-20 year period is a pre-condition to the strategy's ability to succeed.

Any strategy which purports to assist the growth of the local biotechnology industry must address the following issues:

1. The outlook of the academic and research institutions, and particularly the researchers themselves, must be imbued with a more entrepreneurial character. A culture which also rewards commercial applications in addition to scientific advance and scholarship is very much needed. Commercial influences must be brought to bear without impinging on principles of academic freedom and scientific research. The motivation to search for commercial applications of research efforts needs to be further developed at both the institutional and researcher level.

2. Research resources must focus on specific biotechnology areas where Pittsburgh has an edge (or potential edge). Without this focus a critical mass of activity cannot be built with the ability to make substantial progress on complex scientific problems whose solutions have commercial potentials. These resources must be focused in cross-institutional collaborations which take best advantage of the research talent from among each of Pittsburgh's major academic and research institutions. A means of facilitating funding for cross-institutional collaborations is needed.

3. Industry-specific expertise must be recruited and developed to support commercialization efforts, particularly in the areas of proprietary protection, market and competitive assessment, product development and regulatory issues and in licensing and corporate sponsored research promotion and negotiation.

4. Access to commercialization supports and venture development resources must be available to researchers regardless of their institutional setting. Institutional arrangements are necessary which establish central community-wide resources for analysis, promotion, and commercialization (including licensing) of research activities with the support of each of the major academic and research institutions. This centralization can be accomplished while respecting each institution's licensing and commercialization policies. Duplicating the specialized expertise for each institution is likely to be an arduous task.

COMPONENTS OF THE STRATEGY

The recommended components of Pittsburgh's biotechnology strategy are three-fold.

1. Develop Centers of Excellence in core research areas in which Pittsburgh has an advantage. Centers of excellence are characterized by a significant number of researchers (often 40-50, or more) focused on a central scientific problem, with superior scientific leadership in its particular field.

2. Establish targeted commercialization supports to efficiently assess the commercial prospects of innovations and move them into the marketplace. Commercialization supports include the provision of specialized talents which can: identify commercial potentials; quickly assess an innovation's market and competitive position; assist in obtaining appropriate proprietary protection for the innovation; and assist in identifying and recruiting corporations interested in sponsoring research or licensing the technology.

3. Create the venture development capacity for biotechnology start-ups. The venture development tools needed include the provision of pre-seed capital and management assistance in developing business plans, lining up other sources of financing and recruiting management.

Each of these components will be necessary for the growth of Pittsburgh's biotechnology industry. By having each of these components in place, the capacity to transform the existing research base and talents into a bona fide local industry will be developed.

By focusing resources and talents on centers of excellence more scientific progress can be made with commercial potential which in turn will attract more

more research dollars. The result will be more commercializable innovations. Researchers will have ready access to talents able to assist them in devising a commercialization strategy and promoting the innovations to the appropriate commercial interests. Venture development resources can bring research projects along to a more conventionally investable stage and court the interest of venture capitalists, entrepreneurs, management and entrepreneurially minded researchers in Pittsburgh's biotechnology activities.

If centers of excellence are established without commercialization supports, the commercial spin-offs from the centers will be limited. Without venture development resources and capacity, commercially viable concepts will have a more difficult task of translating into Pittsburgh companies.

Each of the three components of the strategy is discussed in turn below.

CENTERS OF EXCELLENCE

The attributes which characterize a center of excellence are the following:

- Critical mass of researchers with interdisciplinary skills.

  Centers of Excellence may have as many as 10-15 labs of 3-10 researchers each with a range of interdisciplinary skills focused on a central problem.

- Focus on a central problem.

  A center of excellence typically focuses on various aspects of a central problem. Solutions to the central problem are approached by investigators from different vantage points and through different skills.

- A leading researcher to head the effort.

  This leadership function is critical in establishing the center's reputation, marshalling the resources to support the center and in maintaining the focus of the center's activities.

- Development of important proprietary technology

  With the prior three elements in place, a center of excellence must usually develop some proprietary technology and establish scientific

leadership in a particular area in order to attract substantial commercial interest.

Well known centers of excellence include Scripps Clinic where Dr. Michael Lerner heads a large group of researchers focused on developing new vaccines and Memorial Sloan-Kettering's efforts in cancer diagnostics and therapeutics (based on monoclonal antibody technology) headed by Dr. Lloyd Old.

Centers of excellence would serve several functions in developing a biotechnology industry.

- By making substantial progress on scientific problems, they attract the attention of commercial interests.
- This attention can translate into multi-million dollar commitments for corporate sponsored research.
- As proprietary knowledge begins to emerge from the center, interest in it builds among additional corporations, entrepreneurs, venture capitalists and other researchers. This interaction breeds spin-off opportunities for further licensing and venture start-ups.

In Pittsburgh three areas stand out as strong candidates to become centers of excellence.

- Cancer biology and therapy

  The program at the Pittsburgh Cancer Institute is well developed. In effect it is on its way to achieving center of excellence status now. As the focal point for the Eastern Cooperative Oncology Group clinical trials with biological response modifiers, the Pittsburgh Cancer Institute will soon be nationally recognized for its work developing new immunotherapeutics. In addition, the Institute is conducting (or about to start) clinical trials on several proprietary agents developed in Pittsburgh, including agents developed by Dr. John Hiserodt and Dr. Ronald Goldfarb.

  Related basic research programs in molecular biology could also be included in this center of excellence, including studies on cancer gene expression, and the development of whole animal tumor models. This molecular biology work may represent early research for later application in the research and development efforts at the Pittsburgh Cancer Institute.

In terms of commercialization, researchers at the Pittsburgh Cancer Institute have begun discussion of at least one start-up venture, involving commercial development of immunotherapeutic approaches developed in Pittsburgh.

- Diagnostics and therapy based in non-invasive imaging

  This center of excellence embodies the "LIMET Institute" concept of Dr. Gerald Wolf, Director of Pittsburgh's NMR Institute. As envisioned by Dr., Wolf, the LIMET Institute will generate revenues in return for clinical services and for contract research (including animal studies and work on drug design). In addition, diagnostic imaging techniques developed by this center of excellence should be licensable, provided that proprietary protection is obtained. New proprietary agents developed by Dr. Wolf's team could be commercialized either in a start-up venture or via licensing to a commercial partner.

- Biomedical data management networks, workstations, and devices

  The feasibility of this center of excellence depends on allocating resources and structuring interdisciplinary and cross-institutional resources among those working in this area. Funding to free up the time of Dr. David Gur to focus on additional projects in this area will be necessary. The combination of a series of roundtables with appropriate active researchers and starter funding to staff the agenda-setting process could be important initial steps towards establishing such a center of excellence.

To move these centers of excellence forward, several issues need to be attended to. These are:

1. Starter funds for establishing the centers need to be allocated. The amount of starter funds needed for a center is in the range of $350,000 - $500,000. These funds would be used to cover an initial 18 months of the associated costs of the leading researcher's salary, provide for initial staff of the the center (2 researchers and administrative support) and add initial but modest monetary support to existing research efforts in that area.

   The Pittsburgh Cancer Institute does not require starter funds, but may benefit from funds for appropriate further packaging and promotion of

its capabilities to commercial interests. The key start-up tasks for the centers in non-invasive imaging and biomedical data management networks and devices are to designate a leading researcher who can begin to define more clearly the research program to be undertaken (selecting a focus on a central scientific problem), build collaborative efforts among researchers in that area across aspects of the problem and raise resources for a full-scale operation of the center.

2. Public and private funders with an interest in biotechnology may want to collaborate on funding decisions and protocol regarding the start-up of these centers.

3. Leaders within each of these areas will need to be designated or recruited. In this regard, the Pittsburgh Cancer Institute is already under the well regarded leadership of Dr Ronald Haberman and Dr. Ronald Goldfarb. Dr. Gerald Wolf's role at the NMR Institute makes him a logical choice to head that center's efforts. Dr. David Gur's special talents also make him a logical candidate for a similar role in the data management networks and devices area.

COMMERCIALIZATION SUPPORTS

The essential task in the area of commercialization supports is to establish a predictable, accessible and effective system for moving research projects with commercial potential into the marketplace. The functions which are critical to such a system are outlined below:

1. Consistent interaction with research efforts to identify innovations. A technically trained individual(s) is needed who is regularly visiting the labs both to identify research with commercial potential, and, as importantly, to identify new potential commercial applications for existing research. The skills of this individual(s) should include the ability to evaluate the stage of development of the research, to determine how far and through what process (on a technical level) does it need to go before commercialization, and what potential exists for commercial applications.

   This function could exist on either a community-wide basis or within each institution. If it were established on a community-wide basis, pre-determined confidential disclosure policies would have to be worked out with each institution.

2. Establishment of specific project priorities to focus the available commercialization supports on the most promising projects.
The means for this function could again be either a capacity within each institution or on a community-wide resource basis.

3. An initial assessment of the proprietary position, market prospects and technical facets of the priority innovations would then be made. The involvement of appropriate patent counsel, biotechnology market and technical specialists will be required at this stage. The specialized patent counsel capability is not likely to exist in Pittsburgh (there are only 2-3 firms in the nation which specialize in biotechnology proprietary protection) and arrangements with an outside firm will be necessary for this function. Pittsburgh should recruit the market and technical specialists necessary to make this process work. These functions are probably best performed on a community-wide basis. It will be difficult for each institution to recruit the specialized skills needed.

4. Devise a commercialization strategy for the innovation.
For those innovations which receive a favorable assessment, a commercialization strategy would be devised which would include:

   a. the next technical steps in the innovation's development which are necessary for commercialization.

   b. a preliminary decision on the avenue commercialization would take. The typical alternatives are:

      - Corporate sponsored research grants, under which academic researchers receive immediate funding for their ongoing research activities, and the sponsoring corporation receives an option to an exclusive license to technology developed with corporate funding. Because funding for National Institutes of Health (NIH) grants, the traditional source of support for basic and clinical research in biomedical areas, is being cut back, many researchers view corporate sponsored research grants as their top priority.

        Sponsored research contracts must be negotiated carefully, and should specify terms under which technology will be licensed to assure maximum return to the university or research institution. Licensing fees and royalties are

usually lower for sponsored research than for straight outlicensing.

- Licensing technology, on either an exclusive or nonexclusive basis, to established corporations that will develop and market products based on the technology. In return for rights to proprietary technology, the academic institution will typically receive license issue fees ranging from $10,000 to $50,000, minimum annual royalties ranging from $5,000 to $20,000, and 1% to 3% royalties on product sales.

- Licensing technology to the university researcher, who will be involved in starting up a new venture to commercialize his or her invention. The academic researcher may be involved on a part time basis to provide technical guidance, may take a one-year sabbatical to get the new company off to a good technical start, or may leave the academic institution to dedicate full-time to the new venture. Though licensing terms are likely to be the same as for established commercial firms, the risk to the university is much higher, since the new firm has no record for successful product development and marketing.

c. a plan to raise resources through corporate sponsored research, commercial development grants, or pre-seed capital funds to finance the commercialization strategy.

It is important that the commercialization strategy adopted for Pittsburgh's biotechnology and bioengineering programs address the needs of the researchers involved. While new start-up ventures are a desired community goal, this is not necessarily the best avenue of commercialization for each innovation. Licensing to established companies is a more appropriate commercialization vehicle for certain innovations.

5. Review of innovations and their commercialization strategies with commercial review panels composed of corporate, venture capital, technical and entrepreneurial interests. Panels convened 3-4 times a year to review Pittsburgh's latest innovations will provide valuable feedback to the researchers and those working with them.

6. Provision of commercial development grants and pre-seed capital funding to the most promising innovations.

In order to implement the commercialization strategies which emerge from the assessment and commercial panel review process described above, two types of financing are recommended — commercial development grants and pre-seed capital investment funds.

Commercial development grants would be used to support the research and other steps necessary to develop an innovation to the point where its commercial potential and prospects for proprietary protection are much better understood. Typical tasks to be financed by commercial development grants would include efforts to reach specific research and development milestones (prototypes of devices, early tests of validity, and so forth), obtain a clearer picture of the proprietary position (competing patents, type of patent to be sought, and so forth) and specific market potential of the innovation (competition from direct and indirect sources, approximate market size and pricing, and which corporations would be interested) and identify any regulatory hurdles to be overcome. Commercial development grants should have as one of their primary outcomes a feasibility decision whether to proceed with further development of the innovation — in essence a go/no go decision. If a decision is reached to move forward with further development, a direction would then be chosen to aggressively pursue one of the following options: corporate-sponsored research funding, licensing to corporate interests, or to begin the process of developing a new venture. Commercial development grants could be structured to provide for a very modest return to the funder. However, such very early stage development funds cannot expect market rates of return. One approach is to build a recoverable grant feature into the commercial development grant concept. When innovations funded with commercial development grants successfully move into the market place a repayment of the grant funds could be triggered. The repayment of the grant could be made over time and the amount of repayment tied to sales, licensing fees or other measures of the innovation's market performance.

Pre-seed capital funds would be used to fund pre-start-up and start-up tasks for new Pittsburgh-based biotechnology ventures and for pursuit of licensing agreements with corporate interests. In return, the pre-seed capital investors would expect a reasonable return on their investments through a stake in the new venture or a participation in licensing fees and royalties.

Commercial development grants are envisioned as providing the resources to position innovations for commercialization. The role of pre-seed capital funds differs in that it is intended to finance the effort to bring commercialization to fruition.

7. Licensing promotion and negotiation assistance.
Whether provided through pre-seed capital resources or as an ongoing service by a supporting organization (or research institution), a strong capacity to seek out potential licensees, promote Pittsburgh's innovations and assist in negotiating license agreements for the research institutions is needed. The network of contacts in the biotechnology area is fairly specialized. Pittsburgh should recruit an individual with knowledge of and experience within this network. This function can be readily designed to comply with the terms and framework of each cooperating institution's licensing policy. In return for this service the institutions could grant the organization providing this function with a limited share of licensing fees.

In the area of commercialization supports the Center for Biotechnology and Bioengineering at the University of Pittsburgh has plans to add staff knowledgeable in technology transfer and commercial applications in biotechnology. The Allegheny-Singer Research Institute and Carnegie Mellon University have also increased their efforts in this regard over the past year. However, the area of commercialization supports needs additional resources, talents and organization to put in place a predictable and reliable protocol for biotechnology commercialization.

VENTURE DEVELOPMENT CAPACITY

To complement the commercialization supports described above and to encourage the start-up of Pittsburgh-based firms , the following capacities should be put in place:

1. Start-up and pre-start-up management assistance in: devising business plans, raising and structuring financing and possibly lining up initial sales.

2. Management recruitment for top and key middle management positions for start-up firms.

3. Pre-seed capital to demonstrate commitment to the venture beyond the assistance provided; signal a willingness to support the venture to other investors and to attract entrepreneurs to Pittsburgh's opportunities.

These venture development capacities are among those presently being developed by the organizers of the Pittsburgh Biomedical Development Corporation.

IV. NEXT STEPS

For the strategy to move further towards implementation we would recommend that the URA and WPATC consider the following:

1. A process for designating and providing start-up funding for Centers of Excellence is needed. URA and WPATC should consider convening leading researchers from among the proposed centers of excellence to discuss how the centers could be formed and funded.

2. A predictable and reliable protocol for commercial assessment, proprietary protection and licensing with the required industry-specific expertise is needed.

   The efforts of the Center for Biotechnology and Bioengineering and the Pittsburgh Biomedical Development Corporation should be funded to provide commercialization supports and venture development capacity to researchers regardless of their institutional setting. Further discussions and experience among these two supporting organizations and the major research institutions should be encouraged to work out policy issues such as licensing promotion and negotiations, ease of collaboration among researchers from different institutions, and proprietary protection.

3. Commercial development grant and pre-seed capital funds need to be secured. WPATC should consider specifically designating a portion of future Ben Franklin grant funds for these purposes.

4. A considerable degree of collaboration may be appropriate among the public, philanthropic and private sector investors with an interest in the strategy to provide the resources and direction for it to succeed. URA and WPATC should consider convening major current and potential funders of the strategy to generate interest and discussion on its implementation.