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Novartis Institutes for Biomedical Research (NIBR)

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Abstract

The Novartis Institutes for Biomedical Research (NIBR) take a unique approach to pharmaceutical research. At the earliest stages, research priorities are determined by patient need and disease understanding with physician-scientists removing the boundaries between research and clinical practice. The NIBR use proof-of-concept (PoC) clinical trials to assist Novartis to find and advance the most promising drug candidates (NIBR, 2011). NIBR's success arises from the ability of researchers from different disciplines to successfully communicate with each other.

The research institutes of the NIBR network are located across the globe to gain access to the world's best scientific talent. The NIBR institutes are strategically located at the following sites: Cambridge US (serving as the headquarters), East Hanover US, Emeryville US, La Jolla California US, Horsham UK, Basel Switzerland, Siena Italy, Shanghai China, and Singapore City, Singapore. This network of institutes encourages teams and individuals to work across institutional and geographic boundaries.

Nearly nine years later, while other companies are scaling back drug development, Novartis' research program is expanding. In 2010 alone, Novartis won Food and Drug Administration approval for four new drugs. The company has nearly 50 drugs in late-stage clinical trials, and in recent years it has roughly doubled the number of drugs that have made it through early-stage trials (Weisman, 2011).

1.0 Introduction

The Novartis Institutes for Biomedical Research (NIBR) take a unique approach to pharmaceutical research. At the earliest stages, research priorities are determined by patient need and disease understanding with physician-scientists removing the boundaries between research and clinical practice. The NIBR use proof-of-concept (PoC) clinical trials to assist Novartis to find and advance the most promising drug candidates (NIBR, 2011). The primary objective of a PoC study is to test hypotheses of how a drug may work in the body and to expedite the generation of clinical evidence regarding patient benefit. The successful outcomes of these PoC trials at NIBR have been attributed to the multidisciplinary teams as well as the collaborations with several partners around the world (NIBR Brochure, 2011). Recognizing the value of scientific advances that are made outside of Novartis, the NIBR actively seeks collaborators with the best technologies and early-stage compounds that complement selected objectives.

2.0 The Partners

In addition to tapping into Novartis' established base, NIBR has developed the policy of establishing and cultivating outside collaborations with academic scientists, clinical investigators, and smaller biotechnology companies (NIBR, 2011). This was a major reason that NIBR headquarters was built in Cambridge. The greater Boston metropolitan area is the home of several top hospitals, universities, and biotechnology companies where ground-breaking basic and clinical research is being conducted. The ability to tap into this network would provide the NIBR a distinct advantage for its own research (Zavoico, 2004).

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the world's best scientific talent. The NIBR institutes are strategically located at the following sites: Cambridge US (serving as the headquarters), East Hanover US, Emeryville US, La Jolla California US, Horsham UK, Basel Switzerland, Siena Italy, Shanghai China, and Singapore City, Singapore. This network of institutes encourages teams and individuals to work across institutional and geographic boundaries. Evidence of this is the use of cross-functional teams with every project including pathways scientists, chemists, disease area specialists, and clinicians. Within NIBR, some groups of scientists specialize in disease areas while others focus on "platforms" – fundamental technologies that apply across a broad spectrum of diseases (Novartis, 2004). Beyond Novartis, through the NIBR Strategic Alliances Group, NIBR has established productive alliances with over 300 collaborators—both academic and industrial (NIBR, 2011). (Figure 1)

At NIBR, the designed research strategy addresses both common and rare diseases. NIBR works to contribute drugs and vaccines for neglected diseases through drug discovery and vaccine research at the Novartis Institute for Tropical Disease (NITD) and the Novartis Vaccines for Global Health (NVGH); contributes to new therapeutic targets, technologies and drug discovery through the Genomics Institute of the Novartis Research Foundation (GNF); and contributes to the discovery of the basic molecular mechanisms of cells and organisms in health and disease through the Friedrich Miescher Institute for Biomedical Research (FMI) (NIBR 2011).

3.0 The Open Innovation Model

NIBR has built expertise around several key technology competencies and diseases.

The Target Diseases and Platforms: Each competency combines automation and robotics, computational science, biology and drug discovery knowledge. By building expertise around key technologies, it can be more effectively applied across diseases that share similar mechanisms. Target disease areas include: Autoimmunity, Transplantation & Inflammation, Cardiovascular & Metabolism, Gastrointestinal, Infectious, Musculoskeletal, Neuroscience, Oncology, Ophthalmology, and Respiratory. (Table 1)

Technological Competency	Description
Analytical Sciences	The Analytical Sciences Group's technological capabilities include the analysis of chemical and biologic compounds as well as structure validation and elucidation.
Biologics	The NIBR Biologics Center (NBC) focuses on the discovery of biologics, primarily antibodies and protein drugs, and more recently, on the discovery of siRNA-based therapeutics.
Biomarker Development	The focus is on safety and efficacy biomarkers for preclinical trials, exploratory clinical studies and clinical development.
Chemistry	The Global Discovery Chemistry (GDC) Group is at the center of drug discovery research at NIBR, focusing on the design and synthesis of potential drug molecules.
Developmental and Molecular Pathways	The Developmental and Molecular Pathways (DMP) Group capabilities are in pathway analysis for target identification/validation including genomics, proteomics, model organisms, high-throughput screening, computational biology and RNAi technology.
Drug Metabolism and Pharmacokinetics	The Drug Metabolism & Pharmacokinetics Team looks at drug behaviors (ADME properties) and assists chemists, preclinical and

Technological Competency	Description
	clinical scientists determine how to optimize the drug for best performance.
Imaging	The Global Imaging Group uses imaging techniques in animal studies for whole body imaging (PET, MRI, CT, and SPECT) and for optical imaging (bioluminescent probes) as well as performs cellular imaging.
Metabolism and Pharmacokinetics	The Metabolism and Pharmacokinetics (MAP) Group analyzes compound optimization and aspects of Absorption, Distribution, Metabolism, and Excretion (ADME). ADME studies provide critical information for deciding which compounds to select for clinical studies or as starting points (leads) for compound optimization activities.
Preclinical Safety	The Preclinical Safety (PCS) Group performs toxicological studies to identify and characterize drug toxicities, describe exposures and establish qualitative and quantitative risks of exposure in humans.
Proteomic Chemistry	The Center for Proteomic Chemistry (CPC) has capabilities in high-throughput screening, preclinical safety profiling, protein structure elucidation, natural products discovery, and protease and kinase research.
Translational Medicine	The Translational Medicine Group guides the design of Proof-of-Concept (PoC) clinical studies, which enable a quick assessment of a compound in a small number of patients against a known (and often rare) disease with a

Technological Competency	Description
	known molecular pathway.

Table 1: NIBR Technological Competencies

Source: NIBR, 2011

The Institutes:

The Novartis Institute for Tropical Diseases (NITD) seeks to treat diseases that afflict patients in the developing world. NITD is a public-private partnership between Novartis and the Singapore Economic Development Board, with more than 100 international scientists based in Singapore. The institute researches novel treatments for major tropical diseases, and provides teaching and training for graduate students and post-doctoral fellows—building capacity to address medical challenges in the developing world. Medicines discovered by the institute are made available at not-for-profit prices to patients who need them. NITD has a strong network of scientific partnerships and collaborations in Singapore and around the world (NIBR, 2011). Partners are instrumental in early research activities, such as target identification and high-throughput screening. For later stages of the drug discovery and development process, as well as outreach to patients, partnerships and alliances are essential to make treatments available in developing countries at low cost (NIBR, 2011).

The Novartis Vaccines Institute for Global Health (NVGH) is a research institute established by Novartis in 2007 and dedicated to the translational research and development of vaccines. The NVGH focuses on diseases that are not receiving adequate attention, especially diseases that are particularly devastating to developing countries. NVGH works in partnership with universities, research institutes and other public and private organizations to develop the science for vaccine development. NVGH bridges the gap between the discovery of promising

vaccine candidates and the manufacturing and distribution of vaccines, by providing the means and expertise for pilot-scale vaccine production and human proof of concept studies. NVGH collaborates with organizations such as the Global Alliance for Vaccines and Immunization, the WHO and UNICEF, and other nongovernmental and non-profit organizations dedicated to working in this realm.

The Friedrich Miescher Institute (FMI) for Biomedical Research is devoted to fundamental biomedical research and focuses on epigenetics, growth control and neurobiology. As part of the Novartis Research Foundation, the FMI is situated at the interface of academic research and biomedical application (FMI, 2011). As an institute of the Novartis Research Foundation, the FMI has extensive experience in the translation of its research findings into downstream application. The FMI has over 50 collaborations with Novartis colleagues at Novartis Institutes of BioMedical Research (NIBR) and within the Genomics Institute of the Novartis Research Foundation - GNF, the Novartis Institute for Tropical Diseases - NITD, and the Novartis Vaccines Institute for Global Health – NVGH (FMI, 2011).

The FMI enjoys an excellent relationship with Novartis and applies a patent policy based on industry standards. Novartis Pharma AG has first right of refusal on IP originating from the FMI. However, there are often findings that Novartis chooses not to pursue and these are available for anyone to exploit. Within the greater Basel area, the FMI interacts with various academic institutions. Scientists from the FMI also cultivate contacts in and contribute to national and international competency networks (FMI, 2011).

The Genomics Institute of the Novartis Research Foundation (GNF) in La Jolla, California, is well-known for excellence in developing advanced technologies, ranging from cellular genomics and proteomics to combinatorial chemistry and structural biology. In addition to its location near the Scripps Research Institute and other international researchers in southern California, the GNF has established scientific collaborations with many external researchers at various academic institutions (GNF, 2011; NIBR, 2011).

The GNF collaborates with a number of non-profit foundations, including the Wellcome Trust and the Medicines for Malaria Venture and has recently announced a partnership with the Juvenile Diabetes Research Foundation. GNF also participates in federally-funded research efforts such as the Protein Structure Initiative as a member of the Joint Center for Structural Genomics (GNF, 2011).

External Collaborations:

Through the NIBR Strategic Alliances Group, NIBR has established productive alliances with over 300 collaborators, both academic and industrial. Collaborators are sought with the best targets, software, assay tools, chemistry, biology, disease models, screening technology, imaging tools and pre-clinical (pre-Proof-of-concept) compounds (NIBR, 2011). Of particular interest are the collaborations in developing markets including with Aurigene in Bangalore India, the Kunming Institute of Botany (KIB) in China, Kyorin in Tokyo Japan, Senju Pharmaceuticals in Osaka Japan, Shanghai Institute of Materia Medica (SIMM) in Shanghai China, and WuXi AppTec in Shanghai China. (Table 2)

NIBR Collaboration in Asia	Focus of Collaboration
Aurigene, India	Generation of small molecules therapeutics against clinical validated targets of interest to

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	Novartis.
Kunming Institute of Botany (KIB), China	Development of new medicines based on extracts from plants and fungi in China.
Kyorin, Japan	Development of a orally active, small molecule agonist of the sphingosine-1 phosphate receptor for the treatment of autoimmune and other diseases.
Senju Pharmaceuticals, Japan	Via sub-license rights granted to Senju for the development of a topical treatment for glaucoma.
Shanghai Institute of Materia Medica, China	Development of new medicines based on extracts from plants in China.
WuXi AppTec, China	Partnership with a custom research organization as a component of broadening reach into China.

Table 2: External Partnerships in Asia
Source: NIBR 2011

4.0 Governance Strategy

Novartis announced in May of 2002 the reorganization of its global pharmaceutical research network into the new Novartis Institutes for BioMedical Research (NIBR) with its new President Mark Fishman. The initial investment included US$250 million, the majority for the creation of a state-of-the-art laboratory space in Cambridge, MA—the new global NIBR headquarters. The greater Boston metropolitan area is the home of several top hospitals, universities, and biotechnology companies where ground-breaking basic and clinical research is being conducted. Hence, the ability to tap into this network was a clear advantage for Novartis (Zavoico, 2004).

Mark Fishman sought scientists who were open-minded and willing to cooperate with each other to streamline the drug discovery and development process and also significantly reduce the risk of failures in late stage clinical trials (Zavoico, 2004). As an example of the cooperation required, Novartis' chemists from all NIBR sites meet regularly to share their knowledge, report on progress, enhance communication, and improve productivity and efficiency (Zavoico, 2004. "We've…created several…. chemistry groups to take advantage of new technologies," said Scott Biller—head of Global Discovery Chemistry at NIBR—"and we've initiated collaborations with a number of biologists at NIBR to assist in identifying novel targets and design molecules that may interact with targets of interest…We're going to do a lot more than just provide a service to biologists," added Scott. "We're creating an international, coordinated, science-based organization that will develop and evaluate innovative approaches to drug discovery and medicinal chemistry." Mark and his strategically hired colleagues are therefore encouraged to foster collaborations with NIBR scientists at all global locations (Zavoico, 2004). (Table 3)

NIBR Location	Focus
NIBR Cambridge, MA	Headquarters
NIBR East Hanover, NJ	Home to Knowledge Center; Home to Information Analysis, Preclinical Safety, Metabolism and Pharmacokinetics
NIBR Emeryville, CA	Key Site for Oncology Research;

NIBR Location	Focus
	Discovery Chemistry
GNF, CA	Cellular Genomics and Proteomics, Combinatorial Chemistry and Structural Biology
NIBR Horsham, UK	Home to Respiratory Research Center; Home to Discovery Chemistry, Biomarker Research, Metabolism and Pharmacokinetics
NIBR Basel, Switzerland	Drug Discovery
FMI, Basel, Switzerland	Epigenetics, Growth Control, Neurobiology
NVGH, Siena, Italy	Vaccines for Neglected Diseases
NITD, Singapore	Treatment and Prevention of Major Tropical Diseases
NIBR, Shanghai, China	Infectious causes of Cancer primarily found in Asia; Discovery Chemistry and Biomarker Research

Table 3: NIBR Global Locations
Source: NIBR, 2011

5.0 Achievements across the NIBR

The success of the NIBR is apparent with 12 PoCs in 2010 (Pathways to Success, 2010). The 12 positive PoCs arose from several disease areas including: Oncology, Cardiovascular and Metabolism, Autoimmunity, Transplantation and Inflammation, Typhoid Fever, Neuroscience, Musculoskeletal, and Gastrointestinal. Dr. Jeff Porter, head of developmental and molecular pathways indicates that at NIBR every project is started with a patient population in mind. "It can really galvanize the team to know where we're going," states Dr. Porter. "That pathway/disease connection is just the starting point. We're aiming for openness and thinking across lines, from pathway to cell, tissue, and organism" (Truelove, 2010).

NIBR's success arises from the ability of researchers from different disciplines to successfully communicate with each other. Unlike in the traditional process where research teams discover promising compounds that are then transferred to the development teams with the drug's effectiveness known only after the development team extensively tests the compound, the NIBR strategy translates to clinical trials and more compounds in development. "There's still a great deal of work to be done, but we get the sense that people are increasingly excited about the way it's playing out," he says. (Truelove, 2010)

To enable collaboration, Mark Fishman initiated the "the lab of the future" (LOTF) program. Fishman hopes to revolutionize the traditional lab bench workspace. "Benches are designed for the way the work was done 50 years ago," states Fishman. "The space isn't used well; at the same time, it's not enough space" (Truelove, 2010) For example, biologists, clinicians, toxicologists and chemists, are historically separated by organizational structure and often in separate areas. Now the core team members will work side-by-side in the LOTF. Furthermore, integrated technology and innovative communications tools will allow scientists to work together both in real and virtual space (Novartis, 2009).

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Mark Fishman said, Novartis Institutes will double the size of a planned office and lab complex in Cambridge, investing $600 million to boost research, and hiring 200 to 300 more employees. That will bring its local workforce to about 2,000 (Weisman, 2011).

Several firms are looking to Novartis now to collaborate on new drug development. "The pathways-based approach…" (that is, encouraging researchers to better understand the molecular pathways that control multiple diseases)…"they've really pioneered at Novartis is one that others are focusing on," said John Maraganore, Alnylam CEO. "You might learn something about pathways in one disease setting that would allow you to use the same or related medicine for other diseases. And that makes the whole drug discovery process more targeted and more efficient" (Weisman, 2011).

With more than 6,000 scientists, physicians and business professionals around the world, the NIBR open innovation model provides valuable lessons for other pharmaceutical firms contemplating opening up their organizational boundaries (NIBR Brochure, 2011).

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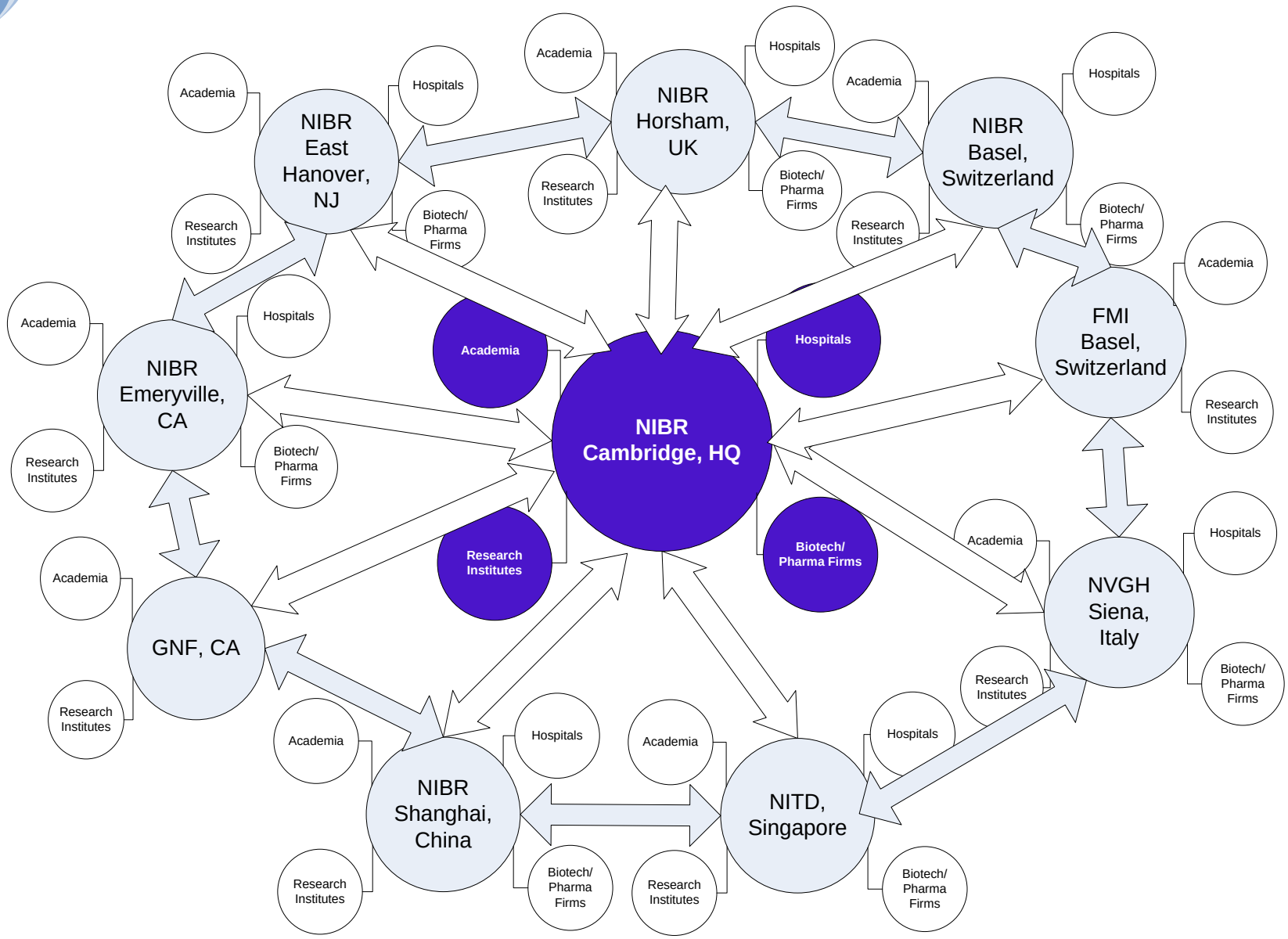

Figure 1: Open Innovation Model at the NIBR