Institute for Applied Cancer Science at UT MD Anderson Cancer Center

Proposed Business and Operating Plan

1. INTRODUCTION

We are continuing to witness significant challenges in our ability to translate fundamental discoveries in cancer biology and genetics towards cures. We have made remarkable improvements in our understanding of the disease and yet - with too few exceptions - therapeutic improvements have been minimal.

The reasons for this failure can be ascribed to both scientific and organizational issues. For many years, we did not have a comprehensive view of the disease's genetics and its complex biology. Much of the advances have been based on anecdotal and accidental discoveries. This resulted in a very limited view of cancer targets and even fewer efficacious drugs, despite the few notable successes. We failed to recognize the importance of modeling the disease in an appropriate setting, limiting our testing to the assessment of anti-proliferative activity in limited poorly genetically-characterized xenograft models. Consequently, there was a lack of predictive value of such testing, resulting in >90% failure rate of compounds in clinical trials that are targeting inadequately validated mechanisms with poorly understood biology. We now appreciate that targeting an oncogene is only efficacious if its gene product is required not just for tumor initiation, but for maintenance of its viability.

Further, we are beginning to gain a more complete understanding of the complex biology of cancer. Historically, our insufficient understanding of the biology of the targets (and the lack of appreciation for such needs) resulted in high failure rate in clinical development, forcing the risk-adverse pharmaceutical industry to focus on generating many candidate drugs directed at the same "me-too" targets.

An additional component that limited the probability of success in achieving significant clinical impact has been the poor preclinical characterization of compounds' pharmaceutical properties, of their metabolic liabilities, and in some cases even their safety profiles, all justified by the need "to accelerate patients' access to potential cures". Over the past twenty or so years, as a result of this thinking, we have subjected millions of patients to unnecessary and ineffective treatments with marginal efficacy. Such has put the survival of Oncology drug discovery and development in pharma in serious peril due to the enormous costs of such operations.

Last but not the least, organizational barriers have hampered progress in translation of discoveries to the clinics. Academia and industry have failed to truly collaborate in drug discovery: academia focusing on causes and industry focusing on remedies, but without ever talking to each other during the process. Furthermore, organizational barriers within industry have created an even more dangerous situation, by separating the responsibilities of those generating candidate drugs (often rewarded solely based on the number of compounds generated) from those in charge of driving their clinical development (rewarded for the number of patients being accrued in trials not for patients having achieved adequate clinical response).

We are now in a position to overcome these issues. The ongoing large-scale cancer genome projects are generating a compendium of somatic alterations in cancers, a critical first-step in understanding and harnessing the cancer genome. Such "parts-list" is providing a large number of target candidates, their connectivity and redundancy are being explored by network

modeling, and cancer relevance being assessed by functional genomics. Along with this emerging view of the complex cancer genome, improved genetic engineering technologies are enabling the generation of cancer models that can appropriately recapitulate key features of their human counterparts. Such models can serve as systems in which one can study tumor and its response to drugs as "neo-organ" growing in appropriate microenvironment. Additionally, biomarker-driven single agent and combination trials in appropriately selected tumor (patient) subpopulations with pharmacogenomics studies will greatly increase the probability of success in clinical development but also enhance our ability to learn from clinical trials. At the same time, drug developers must commit to generating higher-quality drug candidates with superior drug-like properties and evidence of adequate tumor tissue exposure and safety (anticipating combinations).

What we need is new organizational construct that will allow communication and collaboration between industry and academia in order to bring together the tremendous drug discovery capability and the deep biology understanding to increase the probability of conquering cancer. This construct should be embedded with within the rich innovative culture of academic science but populated by scientists whose mission is to systematically enlist the entire compendium of cancer targets into a full array of quality-controlled in vitro and in vivo validation assays designed to validate a gene's cancer relevance and identify the highest potential ones (not just ones that are validated) for drug discovery. With the validation of a novel cancer gene comes the critical challenge of understanding where the target is rate-limiting for tumor maintenance.

Vision and Goals

In complete harmony with MD Anderson's Cancer Center (MDACC) mission to "eliminate cancer in Texas, the nation, and the world through outstanding programs that integrate patient care, research and prevention", the Institute for Applied Cancer Science at MDACC will strive to provide a framework and collaborative environment for delivering new therapeutics to patients. Our goal is to alter radically the survival statistics of several major cancer killers in the next ten years.

The Institute's unique model will be to integrate the best attributes of academic and pharmaceutical science to accelerate translation and drive development of innovative oncology medicines. The Institute's goal of new drug candidates for Phase I testing (Investigational New Drugs, INDs) will be achieved by a combination of internal efforts and collaborative partnerships with industrial partners.

The Institute will drive the translation of basic discoveries to therapeutic endpoints by achieving the following goals:

- Discover basic scientific knowledge specific to cancer and cancer therapy;
- Develop efficient means of testing the impact of these discoveries on cancer dependency and select targets possessing the highest potential for effective therapeutic intervention;
- Develop an internal drug discovery program to advance unprecedented targets, for orphan indications and high medical needs.
- Conduct pre-clinical trials to enable rational selection of optimal drug candidates for human testing;
- Work with an internal business team and governmental, pharmaceutical, and biotechnology partners to move viable drug candidates into clinical trials.

The Institute will be embracing aspects of both academic and industrial research: focus on scientific excellence, teamwork, and hypothesis-driven goal-oriented research. It will bring together scientists with complementary expertise and professional backgrounds in the areas of cancer genomics and bioinformatics, cancer biology and genetics, cancer drug discovery and pharmacology as well as clinical trial expertise. Choices of programs will be driven by unequivocal evidence of their role in disease maintenance in clinically relevant settings.

2. ORGANIZATION

See Appendix I for overall Organizational Chart.

The institute will establish key research units and platforms, each with expertise and specialized capabilities in specific areas that are relevant to different phases of drug discovery. These units will be highly integrated, functioning as one team held together by a matrix that is the platforms which support the activities with complementary expertise. The following general areas will be established at the beginning of the institute.

Scientifically, the institute will be guided by its academic faculties who are committed to its mission and approaches. These faculties will reside primarily in a new Department of Genomic Medicine, chaired by Dr. Lynda Chin. These faculties will be the primary scientific advisers, and are expected to bring to the Institute expertise in areas relevant to drug discoveries, such as genomics, computational biology, signaling, immunology, pharmacology, chemistry, etc.

2.1. Cancer Genomics and Computational biology

Scientists will leverage the information available through the global genome efforts that are being undertaken and expand those efforts by linking available data across disease types and settings, using both human and animal model (mouse) data. The group will contribute to the identification of novel mutations, regions of deletion and amplification, as well as translocations that could become relevant at different disease stages. These findings will aid in the generation of hypotheses for functional validation.

2.2. Target Discovery and Validation

These units' primary focus will be on validating the role of putative cancer targets in tumor maintenance in vivo. Through both gain of function and loss of function approaches in genetically annotated and clinically relevant disease models, scientist will be able to identify candidate targets and further validate them using high-content cell based assays and biochemical assay that will help to establish their role in driving specific phenotypes and pathway mapping.

2.3. Drug discovery Biology: biomarker development

These units will explore key aspects of cancer biology relevant and necessary for drug discovery, such as mechanism-of-action so target-engagement biomarkers can be identified, or rational combinations can be hypothesized. They will also study and explore the complex biology of a target of interest to anticipate possible on-target toxicity associated with inhibition.

2.4. Internal Drug Discovery

This unit will be responsible for internal drug discovery for small or large molecule drugs in the institute. This unit will evaluate existing and available technologies, and identify either

internal (to MDACC) or external (outsourcing) assay development and screening capabilities and build the required infrastructure. It is anticipated that this internal effort will complement corporate alliance relationships where our partners will provide drug discovery capabilities while the institute provides the deep biology required. This will enable the institute (and MDACC) to focus drug discovery effort in area of high unmet needs where corporate industry is unlikely to prioritize, such as orphan indications.

We are mindful of the fact that initiatives in academic drug discovery centers often fall short of delivering clinical candidates with high potential impact in the clinic. We believe that some of the reasons for these failures include:

a. Targets related to faculty's research interests – not necessarily the best or most disease relevant or with highest potential;
b. Poor quality of compounds identified, compounds derived from screens of small, highly-variable sample collections;
c. Lack of understanding on requirements of drug vs. chemical probes;
d. Limited optimization of compounds pharmaceutical properties, often caused by the pressure to advertise one's findings through publication, or by limited viability of technologies and/or funding;
e. Limited consideration about ancillary pharmacology, PK, dosing regimen, required exposures, patient populations, formulation, drug-drug interactions;and,
f. No critical assessment whether compound is fit for market.

To ensure high success probability, we have conducted an in depth analysis of these issues and will aim at the following to address them:

a. Providing an unbiased target selection based on disease relevance and potential impact in the clinic. Our mission is to cure cancer. By design, the institute is not structured to be an extension of any one faculty's research interest;
b. Hiring scientists with pharmaceutical experience to lead drug discovery projects;
c. Establishing multiple platforms for identification of best chemical leads, enable selection of best approaches, providing critical assessment of best compounds; and,
d. Forging partnerships with pharmaceutical industry to provide complementary technical expertise and financial support.

2.5. Integrated Genomics and Biological Annotation Platform

The Institute will build a world-class molecular and biological database of preclinical models based on clinical characteristics. Build a comprehensive molecular and biological reference database that will support both target validation and drug discovery activities, including development of assays. The Unit will also integrate activities of target discovery and validation and drug discovery with "core" and bioinformatics groups to maximize data utilization. These efforts will Increase and maximize utilization of "core" group activities thereby reducing redundancies and increasing productivity of reagent generation/validation through economy of scale.

2.6. Disease modeling, In vivo pharmacology Platforms

These platforms will generate disease maintenance and toxicity (inducible knock-outs, knock-ins, knock-downs) preclinical models for all targets selected to enter deep biology validation for either internal or external drug discovery projects. The platforms will also engineers mouse models of cancer that faithfully recapitulate the genesis and progression of

each of the five cancer types we have prioritized as initial disease programs. We will establish a pre-clinical experimental therapeutics core and conduct pre-clinical evaluation in the general and maintenance models with approximately. Finalization of the above plans will await an analysis of available (both at MNDACC and externally) capabilities.

We will build appropriate cancer models and conduct preclinical trials on such using proof-of-principle antibodies or small molecule inhibitors from above drug development programs. These studies will provide the in vivo system in which to generate and characterize responsive versus non-responsive tumors, as well as eventual resistant tumors. In addition, it will be a system in which biomarkers can be discovered representing distinct phases of tumor evolution. An additional component of the program will be to create an interface with the Small Animal Imaging Facility and the Department of Imaging Physics at MDACC.

3. INSTITUTE LEADERSHIP

Drs. Giulio Draetta and Lynda Chin will co-direct the Institute, providing complementary expertise and skill sets, to ensure that the Institutes retains both components of its integrated strategy for cancer cure. They will be jointly responsible for scientific, operational and financial decisions. Dr. Draetta will report to the Provost's office and Dr. Chin to the Executive Vice Chancellor of The University of Texas System.

Giulio Draetta, MD, PhD, Director

Dr. Draetta is currently Dana Farber Presidential Scholar, Chief Research Business Development Officer and Deputy Director of the Belfer Institute for Applied Cancer Science. Prior to joining the Belfer Institute, Dr. Draetta held appointments at Pharmacia and Merck, as vice-president and worldwide head of oncology drug discovery, and served as an investigator at the Cold Spring Harbor Laboratory, the European Molecular Biology Laboratory in Heidelberg, Germany and at the European Institute of Oncology. During his time in academia, Dr. Draetta spearheaded fundamental research in the biology of the eukaryotic cell division cycle and of DNA damage induced checkpoints. His research led to the discovery of the first mammalian cyclin-dependent kinase and to the demonstration that cyclin-dependent kinases and cyclins physically interact and regulate multiple cell cycle transitions in eukaryotes. Dr. Draetta was also the co-founder and vice president of research for Mitotix, a biotechnology company, where he established programs in cancer, inflammation and infectious diseases that led to successful partnerships with several pharmaceutical companies. During his appointment at Merck, the Oncology research groups initiated a large number of drug discovery programs which led to the generation of 18 clinical candidates, most of which are now in the clinic, including Notch-GSI inhibitors, Aurora inhibitors, MET, PARP and Hedgehog inhibitors and others. During that time, the first Merck Oncology drug, vorinostat (Zolinza®) was also approved. Particular emphasis was given during Dr. Draetta's tenure to the identification of pharmacodynamic and surrogate biomarkers, and most importantly to the genetic identification of potential responder tumor subpopulations (through both human tumor mapping and pathway analysis in model systems). Dr. Draetta received his medical and post-graduate degrees from the University of Naples Medical School, Italy.

Lynda Chin, MD, Scientific Director

Dr. Lynda Chin. Dr. Chin is currently the Scientific Director of the Belfer Institute of Applied Cancer Science, a first of its kind academic construct that aims to bridge the divide between academia and industry. As the Scientific Director of the Belfer Institute, Dr. Chin has been the driver of the scientific foundations for the Institute's current two major corporate alliances (Merck and sanofi-aventis). Dr. Chin is also a Professor of Dermatology at the Harvard Medical School and Department of Medical Oncology at Dana-Farber Cancer Institute, as well as a Senior Associate Member of the Broad Institute of MIT and Harvard. Dr. Chin also co-leads the DF/HCC Melanoma Program and the Harvard Skin SPORE. Dr. Chin received her M.D. from the Albert Einstein College of Medicine in 1993. She is a board-certified dermatologist and conducted her clinical and scientific training at Columbia Presbyterian Medical Center and the Albert Einstein College of Medicine where she served as Chief Resident of Dermatology. Dr. Chin has made multiple scientific discoveries spanning the fields of transcription, mouse models of human cancer, and oncogenomics. Academically, Dr. Chin focuses on mining complex multi-dimensional cancer genomic data and integration with functional genomics to translate these genomic insights into tangible clinical endpoints such as novel therapeutic targets and diagnostic biomarkers. As the Principal Investigator of a TCGA Genome Data Analysis Center and a member of its Executive Subcommittee, Dr. Chin is actively involved in The Cancer Genome Atlas (TCGA) Project. She also chairs the GBM and Melanoma Disease Working Groups that interface the genomic science within TCGA with basic and translational biology in the broader community. Dr. Chin is also a member of the Scientific Steering Committee of the International Cancer Genome Consortium. Dr. Chin has a long history of interest in clinical translation. She has co-founded AVEO Pharmaceuticals in 2002, a cancer biotechnology company that was built on the belief that "genetics will inform the right target to develop the right drug for the right patient". Most recently, Dr. Chin also founded Metamark Genetic, a cancer diagnostic company that will develop function-based prognostic determinants that can guide customized management of early-staged cancer patients. These experiences not only provide her with a deep understanding of the challenges facing drug discovery and development, but also a clear appreciation of the deficiency of the current translational pipeline from academia to industry, hence the need for a new construct.

4. INSTITUTE ORGANIZATION: ADMINISTRATION

4.1. Project Management

The institute will be organized under three function areas: Research, Drug Discovery and Translational Medicine. Within each function area will be units with appropriate and necessary expertise, again supported in a matrix by core platforms. The units in these areas with complementary but specialized expertise must function as a team, driving a program from target discovery to drug development seamlessly. It is also envisioned that the institute will engage multiple corporate partners and relationships at various stages. Due to the magnitude and complexity of these activities, it will be extremely important to proactively manage and coordinate the diverse activities, how they relate to and one can leverage other efforts within MDACC, and to identify future opportunities. Professional project managers will support the co-directors in these activities:

- Monitoring operation and infrastructure deployment ;
- Performance monitoring of all projects in relation to specific milestones;
- Monitoring and project management for corporate collaborations and CROs;
- Facilitation and coordination of activities within the institute and with larger MDACC community;
- Assisting with design and deployment of government and foundation grants and philanthropic sources;
- Assistance with the design and organization of scientific initiatives and meetings relating to disease-related activities; and,
- Personnel management, in coordination with the Department of Genomic Medicine and MDACC Human Resources.

4.2. Intellectual Property Management

A strong intellectual property portfolio of novel proprietary targets, biomarkers and compounds or drugs is essential in enabling their translation and commercialization to the clinics. Therefore, the Institute will have a full time dedicated patent agent who will be embedded into the science within the institute with the goal of securing all possible IP. The Legal Services Department of MD Anderson and the Office of Technology Commercialization will provide counseling on all intellectual property matters and will be responsible for managing intellectual property portfolio of the Institute. Together, the activities will be as follow:

- Provision of legal advisory and management services for Intellectual Property including disclosures, patents, copyrights, trademarks, licensing, and agreements
- Engagement and interaction with internal patent expertise residing in MDACC's legal and tech commercialization offices.
- If necessary, retention of external senior patent attorneys (as strategic advisors) to help develop a strong intellectual property portfolio for the Institute projects
- Identification and evaluation of innovations, including the development of intellectual property protection strategies for such innovations. Using a team approach, internal and external experts will collaborate in drafting and prosecuting patent applications. This approach would have the advantage of having consistent oversight that is focused on the Institute's goals and its IP portfolio while retaining the flexibility to draw on the scientific expertise of a deep pool of experienced patent prosecutors
- Conduct educational seminars on matters of intellectual property, interference proceedings, freedom to operate opinions, infringement avoidance and invalidity opinions, and enforcement of Institute's (and MDACC) policies

4.3. Financial Management

In consultation with the External Advisory Board (EAB), an annual budget will be developed by the co-directors to be approved by the Provost's office. Given the complexity and enormity of the institute's operation, a financial controller will be in place to monitor all expenditures, large and small, in the institute, to ensure that the financial spending is within the approved budget. The controller will also provide projected budget planning support.

The institute's controller will have a dotted line reporting relationship to the MDACC Office of the Chief Financial Officer for appropriate internal control issues regarding the use of institutional funds.

- Development and monitoring of annual capital and operating budgets
- Monthly management reporting and ad hoc financial analysis to support decision making (e.g., investment analysis of key discovery initiatives)
- Financial analysis and oversight for corporate alliance and CRO partnerships

4.4. Business Development

Business development activities will be conducted in coordination with MDACC Office of Technology Commercialization, with consultation with the EAB. Business development activities will include:

- Negotiation and management of all legal agreements to ensure adherence to Institutional policies on such matters;
- Development of strategies to market the unique capabilities and technology offerings of the Institute as a means to attract financial support from the biopharmaceutical industry;
- Negotiation, execution and management of all business agreements with companies that are necessary to establish partnerships with the Institute; and,
- Management of inter-institutional relationships that are likely to emerge as the Institute implements its research plan.

5. INSTITUTE ORGANIZATION: R&D

5.1. Function areas leadership

Three major areas of Functions in the institute will be: Research, Drug Discovery and Translational Medicine. Each area will be led by a Function Head, who will report directly to the Co-Directors. Research will be responsible for the foundational science in this drug discovery enterprise, and is expected to interface with the broader academic environment at MDACC and beyond. Drug Discovery will embark on internal efforts to drive target to drug programs and it will interface and leverage relevant chemistry capabilities at MDACC in addition to its internal or outsourced activities. Translational Medicine will bridge the preclinical to clinical testing in the institute. It will interface with MDACC's deep imaging capabilities and its innovative phase I trial infrastructure. These three function heads will be responsible for ensuring seamless integration across the function areas.

5.2. Unit and Platform leadership

Within each of the Function Areas will be units focusing in different phases of drug discovery, such as target discovery, target validation, target biology and drug discovery biology. These units will have overlapping activities. Each unit will be led by an Associate Director or a Senior Associate Director, who will report to the appropriate Function Head. Core platforms that are supporting diverse activities in multiple units across function areas will be led by Group leaders or Associate Directors and reporting to one function head that is most appropriate.

6. COMPENSATION AND CAREER ADVANCEMENT

Given the construct and the mission of this institute as articulated, it is critical that industry-experienced leadership and staff are recruited to establish the culture of goal-oriented team approaches. Thus, a new track for career advancement and retention is needed that does not fall under the traditional academic ladder. This non-faculty track will be industry competitive and comparable (**See *Appendix II***).

The top level leadership positions are consistent with the framework of current compensation and personnel policies and practices of MDACC (***See Appendix III***). Since these are executive level positions, it is envisioned that they will also qualify for secondary non-tenured track faculty appointments to encourage scholarship and visibility within MDACC and beyond.

Since achievement of the institute (and the R&D staff within it) will be measured in milestones and delivery of new drugs, contributions of the staff to MDACC's overall mission of curing cancer must be evaluated differently from the traditional academic metrics such as publications. Therefore, the institute will reside in a new Department of Genomic Medicine, chaired by Dr. Lynda Chin, which will be the academic home of the Institute and its staff.

7. PERFORMANCE METRICS

We have defined a set of ambitious, yet achievable, goals for the initial 5 years of the Institute's operations. These represent both scientific and business milestones which will ensure long term sustainability of this operation. The projections are based on the Institute's leadership experience with both pharmaceutical research and business development. The financial plan (***See Appendix IV***) outlines the revenue and expenditure projected to achieve the following milestones. Revenues from corporate alliances are projected conservatively based on actual experiences by the co-directors in recent years. Revenues from internal drug discovery programs are modeled conservatively after recent industry examples (***see Appendix V***).

7.1. Milestones

a. In Year 1, recruit key leadership and top scientific talents with industry or industry-like experiences and expertise.

b. Establish laboratory infrastructure in each of the Function Areas.

c. Establish a fully functional Research Area in Year 1 with full complement of capabilities to attract corporate partnerships.

d. Establish one corporate alliance by Year 2, and launch a second corporate alliance in Year 3.

e. Within the first year, establish an internal target validation program leading to the selection of three assay development and hit identification projects, aiming at sustaining a pipeline of three additional screening projects per each subsequent year.

f. Generate 1 small molecule clinical candidate by Year 3 with 1 candidate per year in following years, with the goal of delivering one IND molecule per year starting at Year 5.

g. Execute ONE First-In-Human study in MDACC on a drug developed internally in the Institute by Year 5.

h. Create a strong intellectual property portfolio.

i. Raise $2.5M in philanthropy in Year 1 with a total goal of $42M by end of Year 5.

j. Compete for a foundation or CPRIT grant to support activities in the Institute by Year 2.

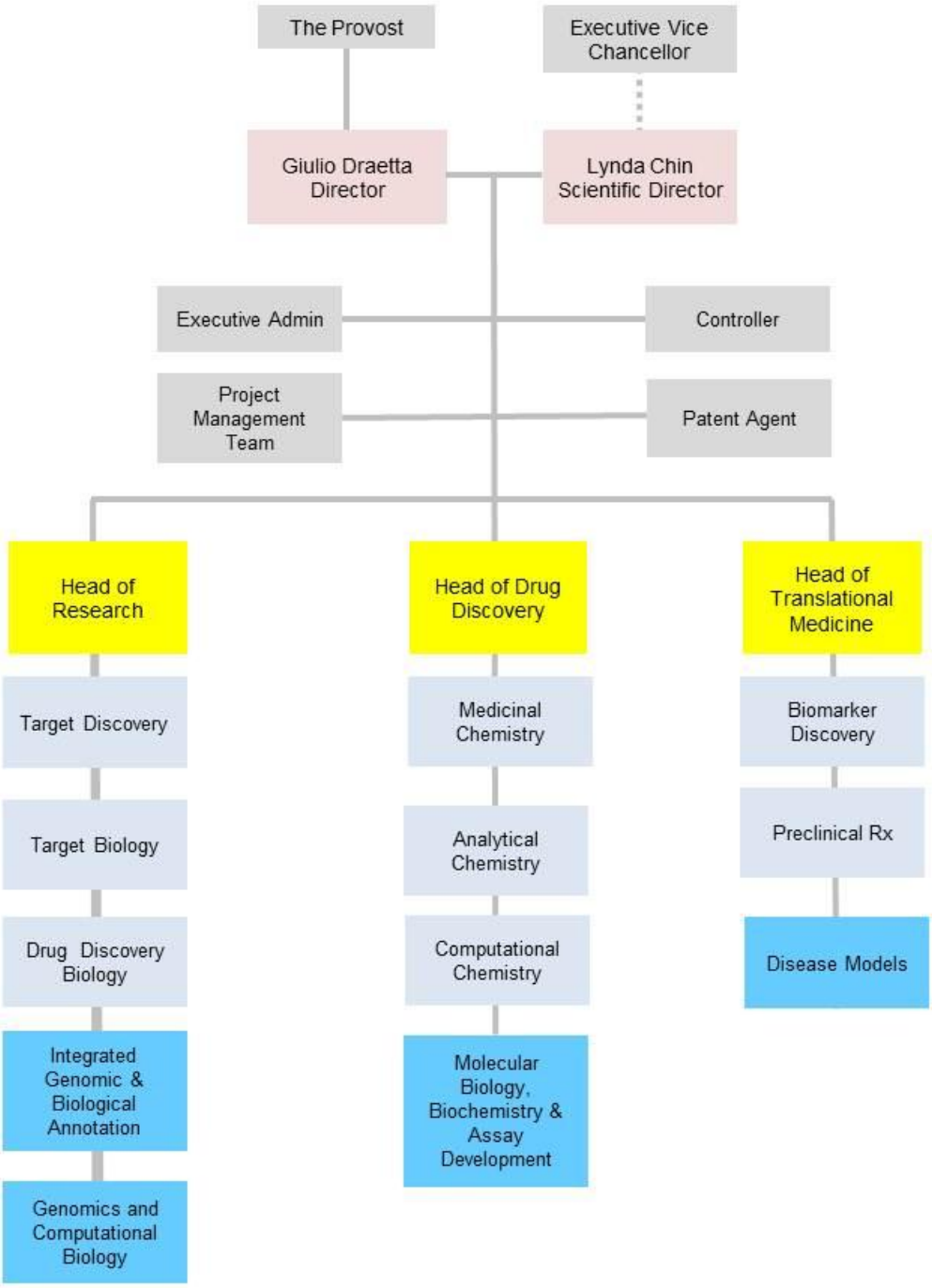
k. Within the first year complete mapping of available technology platforms at MDACC and develop plan for collaborative efforts.

l. Establish a culture of intellectual cross-fertilization between the Institute and the other departments and institutes/centers in MDACC.

8. RESOURCE COMMITMENTS

In addition to the MD Anderson capital investment commitment of $15M per year as outlined in the Financial Plan, appropriate space and support services are required. To start, in Year 1, approximately 10,000 sq ft of laboratory space plus minimum of 5 chemistry hoods will be required to launch the initiatives. Mouse housing capacity of 750 cages will be required. Cumulative needs are projected based on assumptions built based on actual experience of a similar operation at DFCI, ***see Appendix VI***.

Appendix I: Organizational Chart



Appendix II: Industry comparable non-faculty track for recruitment and retention. For details on performance qualifications, see associated excel file.

		Base Salary		Incentive	Total Compensation	
Level	Title	Low	High	%	Low2	High2
1	Research Associate	$35,000	$45,000	10%	$38,500	$49,500
2	Senior Research Associate	$40,000	$55,000	10%	$44,000	$60,500
3	Lead Research Associate	$50,000	$65,000	10%	$55,000	$71,500
4	Principal Research Associate	$60,000	$75,000	10%	$66,000	$82,500
5	Scientist	$70,000	$90,000	10%	$77,000	$99,000
6	Research Scientist	$80,000	$105,000	10%	$88,000	$115,500
7	Senior Research Scientist	$95,000	$120,000	10%	$104,500	$132,000
8	Principal Research Scientist	$110,000	$135,000	10%	$121,000	$148,500
9	Group Leader	$120,000	$170,000	10%	$132,000	$187,000
10	Associate Director	$160,000	$205,000	10%	$176,000	$225,500
11	Senior Associate Director	$195,000	$235,000	10%	$214,500	$258,500
12	Function Head	$240,000	$270,000	24%	$297,600	$334,800
13	Executive Function Head	$270,000	$320,000	24%	$334,800	$396,800

Appendix III: Examples of MDACC position profiles

Position: **Head of Research**
Benchmark: Research Science in pharmaceutical/biotech industry
Total Compensation: $308,000 to $325,000
Target Incentive 1: 4%
Target Incentive 2: 20%
Possible Base Salary: $249,000 to $263,000
Assumption(s):

- Incentive plans may vary based on credentials. PhD credentials assumed for target incentive.
- Associate Vice President position equivalent with Faculty Appointment

Position: **Head of Drug Discovery**
Benchmark: Product Development in pharmaceutical/biotech industry
Total Compensation: $308,000 to $325,000
Target Incentive 1: 4%
Target Incentive 2: 20%
Possible Base Salary: $249,000 to $263,000
Assumption(s):

- Incentive plans may vary based on credentials. PhD credentials assumed for target incentive.
- Associate Vice President position equivalent with Faculty Appointment

Position: **Associate Director, Drug Discovery**
Benchmark: Product Development in pharmaceutical/biotech industry
Total Compensation $192,000 to $225,000
Target Incentive: 10%
Possible Base Salary: $174,000 to $205,000
Assumption(s):

- Incentive plans may vary based on credentials. PhD credentials assumed for target incentive.

Appendix IV. Institute P&L. See associated excel file for details.

Institute for Applied Cancer Science - Financial Operating Plan, FY 2012 - 2016

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
Incremental FTEs						
G&A	2.0	2.0	2.0	0.0	0.0	6.0
Function Heads	2.0	1.0	0.0	0.0	0.0	3.0
Sr. Associate Directors	2.0	1.0	0.0	0.0	0.0	3.0
Associate Directors	2.0	1.0	0.0	0.0	0.0	3.0
Group Leaders	2.0	1.0	0.0	0.0	0.0	3.0
Scientists	10.0	8.0	7.0	4.0	0.0	29.0
Associates	12.0	5.0	5.0	3.0	0.0	25.0
Total # Incremental FTEs	**32.0**	**19.0**	**14.0**	**7.0**	**0.0**	**72.0**

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
Revenue						
Institutional investment	$15,000,000	$15,000,000	$15,000,000	$15,000,000	$15,000,000	$75,000,000
Grants (CPRIT/Foundation)	$0	$2,500,000	$2,500,000	$2,500,000	$2,500,000	$10,000,000
Philantrophy	$2,500,000	$5,000,000	$10,000,000	$12,500,000	$12,500,000	$42,500,000
Corporate Alliances*	$0	$13,000,000	$12,200,000	$9,400,000	$3,650,000	$38,250,000
Other Revenue/Offsets	$0	$0	$10,000,000	$2,200,000	$21,000,000	$33,200,000
Total Revenue	**$17,500,000**	**$35,500,000**	**$49,700,000**	**$41,600,000**	**$54,650,000**	**$198,950,000**
Operating Expenses						
Personnel**	$9,349,000	$14,786,000	$18,711,000	$20,811,000	$20,811,000	$84,468,000
Cancer Genomics	$500,000	$525,000	$551,250	$578,813	$607,753	$2,762,816
Mouse costs	$500,000	$525,000	$551,250	$578,813	$607,753	$2,762,816
Outsourcing costs	$2,000,000	$2,500,000	$3,000,000	$3,000,000	$3,500,000	$14,000,000
Consultants/EAB	$100,000	$100,000	$100,000	$100,000	$100,000	$500,000
Total Operating Expenses	**$12,449,000**	**$18,436,000**	**$22,913,500**	**$25,068,625**	**$25,626,506**	**$104,493,631**
Capital Equipment	$5,000,000	$3,000,000	$2,000,000	$1,000,000	$500,000	$11,500,000
Depreciation	$0	$600,000	$600,000	$600,000	$600,000	$2,400,000
TOTAL COST	**$17,449,000**	**$22,036,000**	**$25,513,500**	**$26,668,625**	**$26,726,506**	**$118,393,631**

TOTAL PROGRAM COST and PROJECTED FUNDING

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
Program Cost						
Capital equipments	$5,000,000	$3,600,000	$2,600,000	$1,600,000	$1,100,000	$13,900,000
Operating Expenses	$12,449,000	$18,436,000	$22,913,500	$25,068,625	$25,626,506	$104,493,631
Total	**$17,449,000**	**$22,036,000**	**$25,513,500**	**$26,668,625**	**$26,726,506**	**$118,393,631**
Projected Funding						
Institution investment *	$15,000,000	$15,000,000	$15,000,000	$15,000,000	$15,000,000	$75,000,000
Projected Revenue	$2,500,000	$20,500,000	$34,700,000	$26,600,000	$39,650,000	$123,950,000
Total	**$17,500,000**	**$35,500,000**	**$49,700,000**	**$41,600,000**	**$54,650,000**	**$198,950,000**
TOTAL PROFIT (LOSS)	**$51,000**	**$13,464,000**	**$24,186,500**	**$14,931,375**	**$27,923,494**	**$80,556,369**

*** Projected revenues when realized will be used to offset institution investment**

Appendix V: Industry comparable for financial revenue projection:

Examples of Recent Early Stage Oncology Deals Providing Favorable Metrics to our Drug Discovery Strategy						
Date	**Biotech**	**Pharma**	**Topic**	**Stage**	**Upfront and R&D support**	**Milestones**
11/08	ArQule	Daiichi-Sankyo	ARQ 197 (c-Met inhibitor) (ex-Asia)	Phase I	60M	560M
12/07	Idera	Merck KGaA	IMO-2055 and IMO-2125 (TLR9 agonists for cancer)	Phase I	40M	335M
08/09	Exelixis	Sanofi	XL147 and XL765 (PI3K)	Phase I	140M	1,000M
12/10	Avila	Sanofi	Undisclosed covalent drug targets	Discovery	40M	154M
10/06	Plexxicon	Roche	PLX4032 (RAF in melanoma)	IND	52M	660M
01/09	Plexxicon	Roche	PLX 5568 (PKD)	IND	60M	275M

Appendix VI: Space projection. For detailed, see associated excel file.

Institute for Applied Cancer Science - Space Plan, FY 2012 - 2016

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
	-	-	-	-	-	-
Incremental FTEs						
G&A	2.0	2.0	2.0	0.0	0.0	6.0
Function Heads	2.0	1.0	0.0	0.0	0.0	3.0
Sr. Associate Directors	2.0	1.0	0.0	0.0	0.0	3.0
Associate Directors	2.0	1.0	0.0	0.0	0.0	3.0
Group Leaders	2.0	1.0	0.0	0.0	0.0	3.0
Scientists	10.0	8.0	7.0	4.0	0.0	29.0
Associates	12.0	5.0	5.0	3.0	0.0	25.0
Total # Incremental FTEs	**32.0**	**19.0**	**14.0**	**7.0**	**0.0**	**72.0**

	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	Total
specialized space						-
mouse housing (cages)	750	250	1000	1000		3000
Chemistry (hoods)	5	10	10			25
Space (Sq ft)						
Genomics & robotics	2000					2,000
G&A	300	300	300	0	0	900
Function Heads	300	150	0	0	0	450
Sr. Associate Directors	300	150	0	0	0	450
Associate Directors	300	150	0	0	0	450
Group Leaders	600	300	0	0	0	900
Scientists	3,000	2,400	2,100	1,200	0	8,700
Associates	3,600	1,500	1,500	900	0	7,500
Total Requirement	**10,400**	**4,950**	**3,900**	**2,100**	**0**	**21,350**

Assumption per FTE, inclusive:		**Breakdown:**	**bench or office need**	**core space utilization**	**total**
Office dry lab space	150		100	50	150
Web lab space	300		150	150	300