

# Institute for Applied Cancer Science

A New Paradigm for High Impact Oncology Drug Development

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## Appendix

### Team

Since late 2011, the IACS has successfully recruited 47 full-time employees (FTEs) to Houston, bringing world-class experience in cancer genomics, bioinformatics, cell biology, animal modeling, drug discovery, in vitro pharmacology, in vivo pharmacology, and medicinal chemistry. The IACS is led by a seasoned team of professionals with cross-functional expertise:

#### **Giulio Draetta, M.D. Ph.D. – Director**

Prior to joining MD Anderson, Giulio Draetta, M.D., Ph.D., was Dana-Farber Presidential Scholar, chief research business development officer and deputy director of the Belfer Institute for Applied Cancer Science at Dana Farber Cancer Institute. Draetta has held appointments at Pharmacia and Merck, as vice-president and as worldwide head of oncology drug discovery. He has 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 also was 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. The company was successfully acquired by GPC Biotech. Over the years, Dr. Draetta led numerous drug discovery and development programs, targeting cyclin-dependent kinases and other mitotic kinases, developmental pathways (Notch, Hedgehog, WNT), receptor tyrosine kinases, AKT and PDK1 kinases, epigenetics and tumor metabolism, which led to two drug approvals in recent years. He recently co-founded Karyopharm, Inc., a biotechnology company focused on the development of selective inhibitors of nuclear export in Oncology and other disease indications. The company recently filed its first IND in Oncology and will initiate clinical trials in both Europe and the USA in 2012. Dr. Draetta is also an advisor to biotechnology and large pharmaceutical companies, including Forma Therapeutics, Blueprint Medicines, Taiho Pharmaceuticals and others.

Dr. Draetta earned his medical and post-graduate degrees from the University of Naples Medical School, Italy.

Dr. Draetta also is professor of Genomic Medicine at MD Anderson.

#### **Lynda Chin, M.D.– Scientific Director**

Lynda Chin, M.D., joined MD Anderson in September 2011 as chair of Genomic Medicine and as scientific director of the Institute for Applied Cancer Science.

For 14 years prior to joining MD Anderson, Dr. Chin was a member of the Dana-Farber Cancer Institute and Harvard Medical School community in Boston. She was professor of Dermatology at Harvard Medical School, member of the Department of Medical Oncology at Dana-Farber Cancer Institute, and senior associate member of the Broad Institute, where she was principal investigator of the Genome Data Analysis Center in The Cancer Genome Atlas (TCGA). Chin also served as scientific director of the Belfer Institute for Applied Cancer Science and co-leader of Dana-Farber/Harvard Cancer Center's Melanoma Program and the Specialized Programs of Research Excellence (SPORE) grant for skin research. She serves on the scientific steering committee of the International Cancer Genome Consortium.

Dr. Chin received her M.D. from the Albert Einstein College of Medicine, followed by clinical and scientific training at Columbia Presbyterian Medical Center and the Albert Einstein College of Medicine, where she was chief resident of dermatology.

She has made multiple scientific discoveries spanning the fields of transcription, telomere biology, mouse models of human cancer, oncogenomics and personalized cancer medicine. Using telomerase-knockout mice, she conducted the first cancer studies, which demonstrated that, in a p53 deficient setting, deactivated DNA damage signaling unleashes a telomere-based crisis as a potent mutational mechanism in the development of cancer.

Building on her successful effort to establish oligo-based array-CGH, Chin has championed comparative oncogenomics of mouse and human cancers and its integration with functional genomics to identify novel cancer genes. As a leader in translational genome medicine, she has enlisted these new cancer gene discoveries into productive drug discovery efforts. She has developed function-based prognosis determinants, solving the longstanding clinical problem of identifying the subset of early-stage melanoma patients who are hardwired for lethal progression. This opens the opportunity for adjuvant therapy for the first time. She serves on the TCGA executive subcommittee and is actively involved in enabling the community to translate genome data via her establishment of “disease working groups” that bring together genome scientists, biologists and clinicians in the broader community. She chairs the glioblastoma multiforme working group and the melanoma disease working group.

Dr. Chin co-founded AVEO Pharmaceuticals in 2002, a cancer biotechnology company that emphasizes cancer biology and genetics to identify new targets with tumor maintenance roles. Most recently, she founded Metamark Genetics, a cancer diagnostics company developing function-based prognostic assays to guide customized care of cancer patients with early-stage disease, including melanoma and prostate cancer.

#### **Carlo Toniatti, M.D., Ph.D. – Head of Research**

Carlo received an M.D. degree at the University of Naples, Italy and a Ph.D. in Molecular and Cellular Biology and Pathology at the University of Naples, Italy

Carlo Toniatti joins the Institute for Applied Cancer Science as Head of Research after more than twenty years of experience in basic research, drug discovery and clinical development in both a biotech and a pharmaceutical company environment. He has significant expertise in Oncology but also in Gene Therapy and RNA-interference, Recombinant Growth Factors and Transcriptional Regulation.

Throughout his career Carlo successfully led multiple programs and cross-functional teams and has gained significant experience in leading different oncology drug discovery programs – including PARP, Wee1, Chk1 and HDM2 inhibitors programs - from target identification/validation to clinical phase 1-2 and in executing on translational research for the therapy of biomarker-defined tumor subtypes. He is also experienced in the management of external collaborations and alliances and in portfolio management.

#### **Philip Jones, Ph.D. – Head of Drug Discovery**

Philip Jones, Ph.D., has more than a decade of drug discovery research experience from Merck Research Laboratories at three locations worldwide. During his career, Jones has led several of Merck’s oncology drug discovery programs, overseeing cross-functional project teams that have successfully delivered novel candidates into ongoing clinical trials. These include Merck’s PARP inhibitor, smoothed antagonist and several HDAC programs, as well as several undisclosed targets. Jones also was involved in the successful development of Raltegravir, the first-in-class HIV integrase inhibitor. He has extensive drug discovery experience across a broad range of target families and has coordinated research across the entire preclinical spectrum from target identification to lead optimization.

Jones received his Ph.D. in organic chemistry from the University of Nottingham, United Kingdom, and completed his post-doctoral research in the laboratory of Professor P. Knochel at Philipps-Universität Marburg, Germany.

### **Eric Devroe, Ph.D. – Executive Director, Strategic Alliances**

Eric Devroe, Ph.D., joins MD Anderson with extensive experience in launching and building new life science enterprises. At the Institute for Applied Cancer Sciences, he focuses broadly on business and strategy development as well as managing the institute's finances. Prior to joining MD Anderson, he was the founding employee and vice president of Business and Strategy Development at Metamark Genetics, Inc., an oncology-focused molecular diagnostics company in Cambridge, MA. At Metamark he oversaw the development of the company's intellectual property portfolio and completed twenty license and partnership agreements, including a \$365 million alliance with Janssen Biotech, Inc. Prior to Metamark he was an associate at Flagship Ventures, a leading life science focused venture capital firm that manages over \$900 million in capital. At Flagship he was a member of the founding team of Joule Unlimited, Inc., and an oncology-focused therapeutics company. Earlier in his career he held scientific and operating roles at Ambion, Asuragen, and Codon Devices. He received his Ph.D. in Biological Chemistry and Molecular Pharmacology from Harvard University.

### **Jannik Andersen, Ph.D. – Senior Associate Director, Drug Discovery Biology**

Jannik Andersen, Ph.D., has extensive expertise in basic and translational cancer research, oncogenic signaling and targeted oncology therapeutics. Prior to joining MD Anderson, he was the associate director of drug discovery at the Belfer Institute of Applied Cancer Science at Dana-Farber Cancer Institute, where he served as the science alliance manager for the corporate partnership with Merck & Co., Inc. Prior to joining the Belfer Institute, he worked for Merck Research Laboratories, where he led early drug discovery programs providing genetic target validation and pharmacological evaluation of lead molecules.

Andersen has authored highly cited original articles and reviews in drug discovery, signal transduction and personalized molecular oncology published in Cell, Nature, Nature Medicine and Science Translational Medicine. He is the principal author of a peer-reviewed website on protein tyrosine phosphatases (PTPs) focusing on sequence analysis, genomics, protein structure and inhibitor design. This original work led to the commercialization of the Expression Arrest™ shRNA library sold by Open Biosystems (RNAi screening).

Andersen has a multidisciplinary educational background with a M.Sc. in chemical engineering from the Technical University of Denmark, as well as a M.Sc. degree in human biology from the University of Copenhagen and a Ph.D. from the Faculty of Medicine, University of Copenhagen, Denmark. He conducted his Ph.D. educational research at Novo Nordisk, training in a world-class signal transduction laboratory focusing on protein phosphatase small molecule drug discovery. Dr. Andersen conducted his post-doctoral studies in the laboratory of Nicholas Tonks, Ph.D., Cold Spring Harbor Laboratory, N.Y.

### **Joseph Marszalek, Ph.D. – Senior Associate Director, Target Validation**

Prior to joining MD Anderson, Joseph Marszalek, Ph.D., led target validation and drug discovery groups at the Dana-Farber Cancer Institute (DFCI). These groups were critical elements of major collaborations with Sanofi-Aventis and Merck. As part of these collaborations, activities from multiple internal and external groups were successfully integrated to enable programs to advance through key pipeline milestones.

Prior to DFCI, he was with Merck Research Laboratories, where he led or was a key member of numerous programs that spanned therapeutic areas and the drug discovery pipeline from early target discovery through compounds in Phase I clinical trials. While Marszalek has a broad range of expertise that crosses many functional and tumor biology areas, much of his oncology research has focused on identifying and validating novel oncology candidates for the development of targeted therapies. In addition, a major focus has been to understand how the tumor microenvironment affects response and confers resistance to therapeutic candidates.

He received his Ph.D. in biomedical sciences from the University of California at San Diego in the laboratory of Larry Goldstein, Ph.D., and completed his post-doctoral research in the laboratory of Harvey Lodish, Ph.D., at the Whitehead Institute at Massachusetts Institute of Technology.

### **James Horner – Associate Director, Mouse Cancer Models**

Together with Ronald DePinho, M.D., James Horner and his facility staff have a long record of mouse engineering and phenotypic characterization of cancer-prone strains. More than 20 years ago, they established the first National Cancer Institute-supported shared transgenic and gene targeting facility at the Albert Einstein College of Medicine. Using early technologies, they generated more than 2,000 different transgenic mouse strains and approximately 200 germline mutant strains for more than 55 different laboratories.

At the Dana-Farber Cancer Institute, this effort was continued with the production of many hundreds of germline transgenic and knock-out/knock-in alleles, the design of which are, on average, far more complex than early generation alleles in the 1990s.

### **Timothy Heffernan, Ph.D. – Associate Director, Target Discovery**

Timothy Heffernan, Ph.D., joins MD Anderson from the Dana-Farber Cancer Institute (DFCI). He is a seasoned cell and molecular biologist with expertise in functional genomics and signal transduction. During his time at DFCI, Heffernan developed proprietary genetic screen platforms that have led to the identification of multiple oncology targets currently in drug development. He was the first to functionalize the cancer genome in high-throughput using engineered models that control for lineage, microenvironmental and genetic influences on gene function. His novel approach to target identity not only informed high priority “context-specific” targets for internal drug discovery, but also served as the basis for corporate alliances with Sanofi-Aventis and Merck Research Labs. In addition to his expertise in target discovery, Heffernan has extensive experience with multidisciplinary groups and has served as project team lead on multiple drug discovery programs.

Dr. Heffernan received his Ph.D. in cell and molecular pathology at the University of North Carolina at Chapel Hill, and completed his post-doctoral training in the laboratory of Lynda Chin, M.D., at DFCI.

### **Alexei Protopopov, Ph.D. – Associate Director, Oncogenomics**

Alexei Protopopov, Ph.D., joins MD Anderson after more than a decade of cancer genetics research at Dana-Farber Cancer Institute (DFCI) and Karolinska Institute, Stockholm, Sweden. During his career, he pioneered and implemented multiple methods of molecular cytogenetics, from fiber-FISH and SKY to microarrays and NextGen Sequencing. He developed new approaches for genomic and epigenetic characterization of tumors, specifically focusing on GEM models, tumor microenvironment and single cell genomics. His research resulted in more than 70 publications in peer-reviewed journals, including Nature and Science.

During his time at DFCI, he led the Arthur and Rochelle Belfer Center for Cancer Genomics and served as a production manager/technical director of The Cancer Genome Atlas' Cancer Genome Characterization Center at Harvard Medical School.

Protopopov received his Ph.D. in biophysics (cell and molecular biology) with Professor Josef Gitelson at the Institute of Biophysics, Russia, trained in tumor biology and completed his post-doctoral research in the laboratory of Professor George Klein at Karolinska Institute, Sweden.

### **Jianhua (John) Zhang, Ph.D. – Associate Director, Bioinformatics**

Jianhua (John) Zhang, Ph.D., has broad training and experience in biology, computer science, biostatistics and bioinformatics. He has made significant contributions to the scientific community worldwide through his involvement and important roles in the bioconductor project (one of the most preferred bioinformatics software archives) that provides cutting-edge bioinformatics tools for the management, process, annotation and analysis of high-throughput biological data. During the past six years, he has been in charge of The Cancer Genome Atlas (TCGA) copy number data processing and analysis production pipeline of the Harvard center. Data processed through the Harvard production pipeline have been published in high impact articles in the journal Nature. Zhang also has been an active developer of modules and contributor of the infrastructure of another successful TCGA related project, the MD Anderson-Broad GDAC that implements analytical tools for analyzing TCGA data and generates high-level analysis results for the scientific community.

## External Advisory Board

The IACS External Advisory Board is composed of recognized leaders in business, science and clinical arenas. Current members are described briefly below with plan to expand before Q2 2012. The Advisory Board meets annually in addition to timely engagement for ad hoc consultations.

### **Raju Kucherlapati**

Dr. Kucherlapati is the Paul C. Cabot Professor of Genetics and Professor of Medicine at Harvard Medical School. Dr. Kucherlapati was the First Scientific Director of the Harvard Medical School – Partners Healthcare Center for Genetics and Genomics (HPCGG). A major goal of HPCGG was to develop and implement strategies for bringing genetics/genomics to clinical medicine. He has been and continues to be active in the national personalized medicine community. He was a Founder of Cell Genesys, Abgenix, Millennium Pharmaceuticals, and Metamark Genetics. Most recently, he has co-founded the KEW Group. As a member of the Board of Directors of these and other companies, Dr. Kucherlapati has gained experience in building highly successful companies from the ground up. Dr. Kucherlapati is a member of the Institute of Medicine of the National Academy of Sciences and the Presidential Commission for the Study of Bioethical Issues.

### **William Helman**

William (Bill) Helman joined the Boston based venture capital firm Grelock Partners Greylock in 1984. As a general Partner at Grelock, he focuses on biomedical and information technology ventures. Bill led Greylock's investments in Zipcar (ZIP), Aveo Pharmaceuticals (Nasdaq: AVEO), Exact Sciences, Upromise (merged with Sallie Mae), Outlooksoft (merged with SAP), Tessera (merged with IXL), Ontogeny (merged with Curis), Hyperion Software (merged with Oracle), Filene's Basement, Pharmacopeia, Millennium Pharmaceuticals (merged with Takeda), Vertex Pharmaceuticals, Mitotix (merged with GPC Biotech) and Reveal Imaging (merged with SAIC).

In addition, Bill serves on the Board of Directors of Ford Motor Company, on the Board of Trustees of Dartmouth College where he serves as Chair of the Investment Committee and on the Board of Harvard Management Company. He is on the Board of the Isabella Stewart Gardner Museum, the Broad Institute, the Damon Runyon Cancer Research Foundation, the Dartmouth Hitchcock Medical Center, and The Steppingstone Foundation and is a member of the Harvard Medical School Board of Fellows.

He is a graduate of Dartmouth College (A.B.) and the Harvard Business School (M.B.A.).

### **Vicki L. Sato, Ph.D.**

Vicki L. Sato, Ph.D, is Professor of Management Practice at Harvard Business School, and also Professor of the Practice in the Department of Molecular and Cell Biology, Harvard University. She also teaches in HBS Executive Education programs. She is a business advisor to Atlas Venture and other enterprises in the biotechnology and pharmaceutical industries.

Dr. Sato retired in 2005 from Vertex Pharmaceuticals, where she served as President since 2000, with responsibility for research and development, business and corporate development, commercial operations, legal, and finance. Prior to becoming President, she was Chief Scientific Officer, Senior Vice President of Research and Development, and Chair of the Scientific Advisory Board. Under her leadership, Vertex created a diversified pipeline of drugs, including two HIV protease inhibitors approved and marketed by GlaxoSmithKline, an oral protease inhibitor (VX 950) for the treatment of hepatitis C, now in late clinical development, two anti-inflammatory drug candidates in clinical development, a novel molecule for the treatment of cystic fibrosis now in Phase I clinical testing, and two kinase inhibitors being for the treatment of cancers. In addition, a new molecule for the management of pain has been recently licensed to GlaxoSmithKline.

Before joining Vertex, Dr. Sato was Vice President of Research at Biogen, Inc, where she led research programs in the areas of inflammation, thrombosis, and HIV disease, and participated in the executive management of the company. Several molecules from those programs have now reached the marketplace. She also served as a member of the Biogen Scientific Board.

Currently, Dr. Sato is a member of the Board of Directors of publicly held companies Bristol Myers Squibb Company, PerkinElmer Corporation, and Alnylam Pharmaceuticals. She is also Chair of the Overseers of the Isabella Stewart Gardner Museum, a founding member of the Board of Scientific Counselors of the Broad Institute, and a board member of Prize4Life, a nonprofit organization focused on finding cures for ALS, founded by HBS alumnus Avichai Kremer.

Dr. Sato received her AB from Radcliffe College, and her AM and PHD degrees from Harvard University. Following postdoctoral work at both the University of California Berkeley and Stanford Medical Center, Dr. Sato was appointed to the faculty of Harvard University, where she was an Assistant and Associate Professor of Biology.

**Webster (Web) Cavenee, Ph.D.**

Dr. Web Cavevve is Professor of Medicine and Cell & Molecular Medicine, Cancer Biology Program at the University of California San Diego and Director, Ludwig Institute for Cancer Research, San Diego. Dr. Cavenee's original research seeking to define the genetic lesions in retinoblastoma led to the first hard experimental evidence for the existence of tumor suppressor genes in humans. This breakthrough confirmed the "two-hit hypothesis," fundamentally altering the way scientists think about the onset of cancer and its progression. Dr. Cavenee is currently working on identifying the regulatory mechanisms of a type of chromosome translocator, the FKHR gene family. Genes in this family code for molecules that play critical roles in the early stage of cell division. Dr. Cavenee is a Fellow of the National Foundation for Cancer Research and has won many honors, including the Charles S. Mott Prize of the General Motors Cancer Research Foundation and the Albert Szent-Györgyi Prize for Progress in Cancer Research by the National Foundation for Cancer Research. He is a member of the National Academy of Sciences, a former president of the American Association for Cancer Research, a Fellow of the American Academy of Microbiology, and serves on the editorial boards of several journals. He has also served on the board of both the Scientific Counselors of the National Cancer Institute and the National Institute of Environmental Health Sciences. Cavenee received his doctorate from the University of Kansas School of Medicine.

**Michael (Mike) Stratton, Ph.D.**

Prof. Stratton is Director of the Wellcome Trust Sanger Institute, where he is joint head of the Cancer Genome Project, which aims to elucidate the genetic causes of human cancers. Mike is also Professor of Cancer Genetics at the Institute of Cancer Research.

He qualified in medicine at Oxford University and Guys Hospital, trained as a histopathologist at the Hammersmith and Maudsley Hospitals and obtained a PhD in the molecular biology of cancer at the Institute of Cancer Research. His research interests have been in the genetics of cancer. He led the group that mapped and identified the high risk breast cancer susceptibility gene, *BRCA2*. More recently he has found moderate risk breast cancer susceptibility genes such as *CHEK2*, *ATM*, *BRIP* and *PALB2* as well as genes for skin, testis, colorectal, thyroid, and childhood cancers. At the Cancer Genome Project he conducts high throughput, systematic genome wide searches for somatic mutations in human cancer in order to identify new cancer genes, to understand processes of mutagenesis in human cancers and to reveal the role of genome structure in determining abnormalities of cancer genomes. These studies have led to the discovery of activating somatic mutations in the *BRAF* and *ERBB2* genes in melanoma and lung cancer respectively and have described basic patterns of somatic mutation in cancer genomes. He was elected a Fellow of the Royal Society in 2008.

Additional members being invited include Texas science and business leaders.

## Revenue Model: Partnership Assumptions

	<i>Timing of Partnership</i>	<b>Upfront</b>	<b>Potential Milestones w/i 18-months</b>	<b>Milestone trigger(s)</b>
<b>Small Molecule</b>	<b>Clinical Candidate</b>	\$5,000,000	\$5,000,000	Tech transfer; IND filing; dosing of first patients in Phase I
	<b>IND-ready</b>	\$15,000,000	\$3,000,000	IND filing; dosing of first patients in Phase I
	<b>After Phase 1/1b initiated</b>	\$20,000,000	\$7,500,000	Completion of enrollment; safety achieved (could consider a tiered milestone if signs of efficacy are observed, but do not incorporate this into assumptions)
	<b>Phase II</b>	\$70,000,000	\$20,000,000	Initiation of Ph III
<b>mAb</b>	<b>Humanized mAb candidate</b>	\$15,000,000	\$10,000,000	BLA
	<b>After Phase 1/1b initiated</b>	\$25,000,000	\$10,000,000	Phase I goals achieved; possibly more if early signs of efficacy, but do not incorporate this into assumptions
	<b>Phase II</b>	n/a as plan calls to partner prior to this stage;		
<b>Any asset</b>	<b>NewCo</b>	\$500,000	\$1,000,000	Capital raise >\$10M; business development transaction raising >\$5M

**Source:** Direct Team experience with comparable deals; internal analysis of oncology partnerships (2009-2012)

## Institute for Applied Cancer Science - Financial Operating Plan, 2012 - 2017

	Sep 2011 - May 2012	June 2012 - May 2013	June 2013 - May 2014	June 2014 - May 2015	June 2015 - May 2016	June 2016 - May 2017	Total
<b>Revenue</b>							
Institutional investment	\$15,000,000	\$15,000,000	\$15,000,000	\$15,000,000	\$15,000,000	\$0	\$75,000,000
CPRIT	\$0	\$25,000,000	\$25,000,000	\$25,000,000	\$0	\$0	\$75,000,000
Philanthropy/Grants	\$100,000	\$2,500,000	\$5,000,000	\$5,000,000	\$10,000,000	\$10,000,000	\$32,600,000
Corporate Partnerships	\$0	\$0	\$5,000,000	\$20,000,000	\$35,000,000	\$35,000,000	\$95,000,000
<b>Total Revenue</b>	<b>\$15,100,000</b>	<b>\$42,500,000</b>	<b>\$50,000,000</b>	<b>\$65,000,000</b>	<b>\$60,000,000</b>	<b>\$45,000,000</b>	<b>\$277,600,000</b>
<b>Operating Expenses</b>							
G&A	\$825,000	\$1,520,000	\$1,932,500	\$2,082,500	\$2,082,500	\$2,082,500	\$10,525,000
Personnel ( <i>Bus Dev, Admins, Patent Agent, Controller, Program Mgmt</i> )*	\$800,000	\$1,300,000	\$1,462,500	\$1,462,500	\$1,462,500	\$1,462,500	\$7,950,000
Outside Legal (incl. IP filing, prosec, and maintenance)	\$25,000	\$100,000	\$350,000	\$500,000	\$500,000	\$500,000	\$1,975,000
External Advisory Board	\$0	\$120,000	\$120,000	\$120,000	\$120,000	\$120,000	\$600,000
R&D	\$5,900,000	\$32,075,000	\$43,950,000	\$49,502,500	\$41,557,625	\$37,115,506	\$210,100,631
Personnel Subtotal (fully-loaded including general research costs)*	\$5,100,000	\$21,075,000	\$24,400,000	\$24,400,000	\$24,400,000	\$24,400,000	\$123,775,000
<i>Function Heads (Biology, Drug Disc, Biologics)</i>		\$975,000	\$1,300,000	\$1,300,000	\$1,300,000	\$1,300,000	
<i>Sr. Associate Directors</i>		\$600,000	\$900,000	\$900,000	\$900,000	\$900,000	
<i>Associate Directors</i>	**	\$1,800,000	\$1,800,000	\$1,800,000	\$1,800,000	\$1,800,000	
<i>Group Leaders</i>		\$1,200,000	\$1,500,000	\$1,500,000	\$1,500,000	\$1,500,000	
<i>Scientists</i>		\$7,500,000	\$8,400,000	\$8,400,000	\$8,400,000	\$8,400,000	
<i>Associates</i>		\$9,000,000	\$10,500,000	\$10,500,000	\$10,500,000	\$10,500,000	
Other Expenditures Subtotal	\$800,000	\$11,000,000	\$19,550,000	\$25,102,500	\$17,157,625	\$12,715,506	\$86,325,631
Mouse costs	\$100,000	\$1,000,000	\$1,050,000	\$1,102,500	\$1,157,625	\$1,215,506	\$5,625,631
-omic Studies (genomics, proteomics, etc.)	\$200,000	\$1,000,000	\$1,000,000	\$1,000,000	\$1,000,000	\$1,000,000	\$5,200,000
Chemistry outsourcing	\$500,000	\$1,000,000	\$1,500,000	\$1,500,000	\$1,500,000	\$2,000,000	\$8,000,000
mAb (Development, Humanization, Scale-up)	\$0	\$1,000,000	\$2,000,000	\$2,500,000	\$2,500,000	\$2,500,000	\$10,500,000
IND-enabling studies***	\$0	\$2,000,000	\$4,000,000	\$9,000,000	\$6,000,000	\$6,000,000	\$27,000,000
Phase I Clinical Trials	\$0	\$0	\$5,000,000	\$10,000,000	\$5,000,000	\$0	\$20,000,000
Asset In-Licensing (non-recurring, strategic expenditure)	\$0	\$5,000,000	\$5,000,000	\$0	\$0	\$0	\$10,000,000
<b>Total Operating Expenses</b>	<b>\$6,725,000</b>	<b>\$33,595,000</b>	<b>\$45,882,500</b>	<b>\$51,585,000</b>	<b>\$43,640,125</b>	<b>\$39,198,006</b>	<b>\$220,625,631</b>
<b>Capital Equipment</b>	<b>\$6,000,000</b>	<b>\$7,500,000</b>	<b>\$3,500,000</b>	<b>\$2,000,000</b>	<b>\$1,000,000</b>	<b>\$500,000</b>	<b>\$20,500,000</b>
<b>TOTAL COST</b>	<b>\$12,725,000</b>	<b>\$41,095,000</b>	<b>\$49,382,500</b>	<b>\$53,585,000</b>	<b>\$44,640,125</b>	<b>\$39,698,006</b>	<b>\$241,125,631</b>

\* See below FTE table for assumptions. For all R&D staff, an industry-standard estimate of \$300k/FTE is used to include salary and R&D costs (consumables, reagents, etc)

\*\* Given partial year and non-synchrony of hiring during initial phase, the expected total allocation is presented in lieu of the annualized \$300k/FTE approximation.

\*\*\* \$3M per clinical candidate

## TOTAL PROGRAM COST and PROJECTED FUNDING

	Sep 2011 - May 2012	June 2012 - May 2013	June 2013 - May 2014	June 2014 - May 2015	June 2015 - May 2016	June 2016 - May 2017	Total
<b>Program Cost</b>							
Capital equipment	\$6,000,000	\$7,500,000	\$3,500,000	\$2,000,000	\$1,000,000	\$500,000	\$20,500,000
Operating Expenses	\$6,725,000	\$33,595,000	\$45,882,500	\$51,585,000	\$43,640,125	\$39,198,006	\$220,625,631
<b>Total</b>	<b>\$12,725,000</b>	<b>\$41,095,000</b>	<b>\$49,382,500</b>	<b>\$53,585,000</b>	<b>\$44,640,125</b>	<b>\$39,698,006</b>	<b>\$241,125,631</b>
<b>Projected Funding</b>							
MD Anderson institutional investment	\$15,000,000	\$15,000,000	\$15,000,000	\$15,000,000	\$15,000,000	\$0	\$75,000,000
CPRIT	\$0	\$25,000,000	\$25,000,000	\$25,000,000	\$0	\$0	\$75,000,000
Philanthropy and Grants	\$100,000	\$2,500,000	\$5,000,000	\$5,000,000	\$10,000,000	\$10,000,000	\$32,600,000
Corporate Partnerships	\$0	\$0	\$5,000,000	\$20,000,000	\$35,000,000	\$35,000,000	\$95,000,000
<b>Total</b>	<b>\$15,100,000</b>	<b>\$42,500,000</b>	<b>\$50,000,000</b>	<b>\$65,000,000</b>	<b>\$60,000,000</b>	<b>\$45,000,000</b>	<b>\$277,600,000</b>
<b>PROFIT (LOSS)</b>	<b>\$2,375,000</b>	<b>\$1,405,000</b>	<b>\$617,500</b>	<b>\$11,415,000</b>	<b>\$15,359,875</b>	<b>\$5,301,994</b>	<b>\$36,474,369</b>
<b>Ending Cash Balance</b>	<b>\$2,375,000</b>	<b>\$3,780,000</b>	<b>\$4,397,500</b>	<b>\$15,812,500</b>	<b>\$31,172,375</b>	<b>\$36,474,369</b>	

	Sep 2011 - May 2012	June 2012 - May 2013	June 2013 - May 2014	June 2014 - May 2015	June 2015 - May 2016	June 2016 - May 2017	
<b>FTEs</b>	-	-	-	-	-	-	-
G&A (Bus Dev, Admins, Patent Agent, Controller, Program Mgmt)*	6	8	9	9	9	9	
Function Heads (Biology, Drug Disc, Biologics)**	2	3	4	4	4	4	
Sr. Associate Directors***	2	2	3	3	3	3	
Associate Directors	6	6	6	6	6	6	
Group Leaders	4	4	5	5	5	5	
Scientists	7	25	28	28	28	28	
Associates	24	30	35	35	35	35	
<b>Total # FTEs</b>	<b>51</b>	<b>78</b>	<b>90</b>	<b>90</b>	<b>90</b>	<b>90</b>	

\* A blended average of \$162,500 = salary + 30% fringe

\*\* \$325,000 = salary + 30% fringe

\*\*\* \$300,000 = fully loaded (salary, fringe, and all reagents and consumables)

## Detailed Use of CPRIT Proceeds – Year 1

	Enhancement of Current Approach		Strategic Expansion Opportunities	
	Small Molecule Pipeline Expansion	BioTherapeutics	Novel Chemistry Platform	In-Licensing
	Summary	Summary	Summary	Summary
<b>FTEs*</b>	5 chemists, 5 biologists, 1 computational biologist; 1 in vivo pharmacologist (\$3,600,000)	1 Head of BioTherapeutics; 4 immunologists; 3 biologists; 2 pharmacologists (\$3,000,000)	8 chemists, 2 biologists; 2 pharmacologists (\$3,600,000)	4 biologists, 2 in vivo pharmacologists, 1 computational biologist (\$2,100,000)
<b>Capital Equipment</b>	Compound screening automation; plate reader; biophysical instruments (ITC and/or Biacore) (\$500,000)	Liquid handlers, dedicated tissue culture suites; ITC; cryostorage small-scale bioreactors; automation for HT mAb purification (\$2,500,000)	Expand analytical chemistry platform (UPLC/MS/MS), liquid handling automation (\$1,000,000)	Leverage existing infrastructure (\$0)
<b>Major Initiatives</b>	Develop in vitro/in vivo platform to study tumor-stroma interaction and evaluate the effect of said interaction on small molecule efficacy; develop screening platform to evaluate drugs and combinations of drugs in an unbiased manner on a panel of 50-60 cell lines (\$1,500,000)	mAb development, sequencing, isotype engineering; development of platform for identification and functional validation of tumor specific antigens and/or evaluate immunomodulators; develop appropriate mouse models to study immunomodulators and/or therapeutic mAbs (\$3,500,000)	Aggressive patent filing efforts upon POC (engage outside counsel); mouse POC work and initial large animal (dogs or primates) studies (\$1,000,000)	Active scouts; due diligence support; clinical path and responder hypothesis generation - deep sequencing, phosphoproteomics (\$2,700,000)
<b>Total</b>	\$5,600,000	\$9,000,000	\$5,600,000	\$4,800,000
<b>Year 1 Total</b>	<b>\$25,000,000</b>			

\* For simplicity, FTE costs are fully-loaded at \$300k/hire (includes salary plus all reagents, consumables required for year of job functions)