Bridging the gap between life sciences academic research, philanthropic support, and venture capital

Manuel O. Lopez Figueroa, Ph.D.

Vice President, Bay City Capital and Scientific Liaison at Pritzker Consortia

UFS, April 26, 2012
Agenda

- Introduction to Bay City Capital
- Overview of the Pritzker Neuropsychiatric Disorders Research Consortium
Introduction to Bay City Capital
Investing in Life Sciences

- Global, diversified strategy ranging from seed to public, including distressed and securitized asset investing

- $1.6 billion in total capital commitments across eight funds
  - $1.45 billion across five general life sciences funds
  - Three additional sector funds

- History of upper quartile performance

- Team longevity

- Broad and deep operating experience

- Lead or co-lead investor

- Over 90 companies funded since 1997
# Capital Commitments

## GENERAL LIFE SCIENCES FUNDS

<table>
<thead>
<tr>
<th>Fund</th>
<th>Vintage Year</th>
<th>Capital Committed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bay City Capital Fund V</td>
<td>2007</td>
<td>$ 500M</td>
</tr>
<tr>
<td>Bay City Capital Fund IV</td>
<td>2004</td>
<td>351M</td>
</tr>
<tr>
<td>Bay City Capital Fund III</td>
<td>2001</td>
<td>252M</td>
</tr>
<tr>
<td>Bay City Capital Fund II</td>
<td>1999</td>
<td>201M</td>
</tr>
<tr>
<td>Bay City Capital Fund I</td>
<td>1997</td>
<td>148M</td>
</tr>
</tbody>
</table>

$1,452M

## SECTOR FUNDS

<table>
<thead>
<tr>
<th>Fund</th>
<th>Vintage Year</th>
<th>Capital Committed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decheng China I</td>
<td>2011</td>
<td></td>
</tr>
<tr>
<td>Birchmere Ventures III</td>
<td>2005</td>
<td>$ 47M</td>
</tr>
<tr>
<td>North American Nutrition &amp; Agribusiness Fund (NANAF)</td>
<td>1999</td>
<td>111M</td>
</tr>
</tbody>
</table>

Capital commitments of Funds I, II, and III include co-investments by Pritzker family business interests.

Capital commitments of Funds II, III, IV, V, and BV3 include respective side funds.
### Deep Domain Expertise: Therapeutics, Diagnostics, and Devices

**Indications pursued by Bay City Capital’s portfolio companies**

<table>
<thead>
<tr>
<th>CARDIOVASCULAR</th>
<th>ONCOLOGY</th>
<th>METABOLIC DISORDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute MI</td>
<td>acute leukemia</td>
<td>diabetes</td>
</tr>
<tr>
<td>atherosclerosis</td>
<td>breast cancer</td>
<td>hepatic encephalopathy</td>
</tr>
<tr>
<td>atrial fibrillation</td>
<td>colorectal cancer</td>
<td>obesity</td>
</tr>
<tr>
<td>cholesterol reduction</td>
<td>melanoma</td>
<td>sleep disorders</td>
</tr>
<tr>
<td>coronary artery disease</td>
<td>multiple myeloma</td>
<td></td>
</tr>
<tr>
<td>dyslipidemia</td>
<td>myelodysplastic syndrome</td>
<td></td>
</tr>
<tr>
<td>endothelial dysfunction</td>
<td>ovarian cancer</td>
<td></td>
</tr>
<tr>
<td>high triglycerides</td>
<td>prostate cancer</td>
<td></td>
</tr>
<tr>
<td>hypertension</td>
<td>small cell lung cancer</td>
<td></td>
</tr>
<tr>
<td>peripheral arterial stenosis</td>
<td>other solid tumors</td>
<td></td>
</tr>
<tr>
<td>radiocontrast nephropathy</td>
<td></td>
<td></td>
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<tr>
<td>vascular inflammation</td>
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</table>

<table>
<thead>
<tr>
<th>OPHTHALMOLOGY</th>
<th>CNS</th>
<th>GENETIC DISORDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>age-related macular degeneration</td>
<td>acute pain</td>
<td>cystic fibrosis</td>
</tr>
<tr>
<td>front of the eye diseases</td>
<td>anxiety</td>
<td>hemophilia</td>
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<tr>
<td>glaucoma</td>
<td>attention deficit disorder</td>
<td>muscular dystrophy</td>
</tr>
<tr>
<td>macular edema</td>
<td>chronic pain</td>
<td>urea cycle disorder</td>
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</table>

<table>
<thead>
<tr>
<th>INFECTIOUS DISEASES</th>
<th>PLATFORM TOOLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>hepatitis C</td>
<td>assays &amp; kits</td>
</tr>
<tr>
<td>HIV</td>
<td>clinical trials testing</td>
</tr>
<tr>
<td>influenza</td>
<td>gene expression modulation</td>
</tr>
<tr>
<td>community-acquired pneumonia</td>
<td>genomic sequencing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SURGICAL TOOLS</th>
<th>RESPIRATORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>general surgery</td>
<td>asthma</td>
</tr>
<tr>
<td>open hysterectomy</td>
<td>COPD</td>
</tr>
<tr>
<td></td>
<td>sleep apnea</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DERMATOLOGY</th>
<th>ONCOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>acne</td>
<td>acute leukemia</td>
</tr>
<tr>
<td>Inflammatory skin diseases</td>
<td>breast cancer</td>
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<td>migraine</td>
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<tr>
<td>obesity</td>
<td>schizophrenia</td>
</tr>
<tr>
<td>sleep disorders</td>
<td></td>
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</table>
Broad Spectrum of Investments

**Sector – By $ Amount Invested**
- BioPharma: 52%
- Med Device: 14%
- Med Dx: 7%
- Nutrition/Ag: 7%
- HCIT: 6%
- Tools/Services: 3%
- Drug Discovery: 11%

**Initial Stage – By # of Companies**
- Seed: 11
- Early: 36
- Mid: 22
- Late: 8
- Public: 11
- Fund: 2

- Transaction types: Create NewCos, Traditional VC, Turnaround/Restructuring, Public
- Areas of strategic interest: Innovation, Emerging Markets, Growth Capital
Financing Healthcare Innovation: a Paradigm Shift in the Environment
Due to significant unmet medical needs, most drugs that received approval yielded substantial profits to justify the risk of investment.

- Life sciences innovation primarily originated from basic research conducted in university and government institutions.
- Translating innovation from basic research into drug candidates was for the most part funded by the venture capital industry.
- As development progressed, risk was reduced and expenses increased.
- A funding shift occurred from venture capital to public investors and large pharma.

VC served as an engine for translating research into pharma projects.
# The Current State of the Healthcare Industry

<table>
<thead>
<tr>
<th>Innovation</th>
<th>Translational Research</th>
<th>Development I</th>
<th>Development II</th>
<th>Development III</th>
<th>Regulatory Approval</th>
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<tbody>
<tr>
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<td>PHARMA</td>
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<tr>
<td>GOVT</td>
<td>VENTURE</td>
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</tbody>
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## Problem:
**“Valley of Death”**

- Innovation is still generated by universities and government
- Pharma research funding has decreased
- Venture funding has decreased
- Growing cache of untapped innovative discoveries
- More complicated and conservative regulatory environment
  - Larger size, complexity, and cost associated with clinical trials in US/EU
  - Pharma, public investors, VC are increasingly risk averse;
  - Public investors have abandoned development stage companies; VCs are stuck/leaving
  - Pharma is focusing on commercial opportunities
  - Development funding is decreasing and being exported

## Result:
Fewer innovative projects are moving into pharma

- US healthcare reform – Pricing affected by proof of improved outcome and cost benefits (Innovation)
- Pharma blockbuster products facing patent cliffs
- Still many areas of unmet medical need
- Pharma sales growth: <5% in developed countries and >20% in emerging markets
Exploiting Opportunities Within the New Paradigm

Rather than handing off assets from one stage to the next and hoping that the final product is desired by pharma:

1) Unite academia, pharma partners, and venture funding

2) Transform innovation into commercial opportunities that fulfill the needs of the pharma industry

3) Leverage a capital efficient (virtual) model with operational and strategic advantages from offshore operations

4) Focus on liquidity
Integrating Stakeholders to Address the “Valley of Death”

CURRENT CHALLENGE

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Translational Research</th>
<th>Development</th>
<th>Regulatory Approval</th>
<th>Marketed Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACADEMIA</td>
<td>VENTURE</td>
<td>PHARMA</td>
<td>PHARMA</td>
<td>PAYORS</td>
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<tr>
<td>GOV’T</td>
<td>ACADEMIA</td>
<td>VENTURE</td>
<td>PUBLIC MKTS</td>
<td>PROVIDERS</td>
</tr>
<tr>
<td></td>
<td>GOV’T</td>
<td>ACADEMIA</td>
<td>VENTURE</td>
<td></td>
</tr>
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BAY CITY CAPITAL’S APPROACH
Bay City Capital Solution: Integrate and Align Stakeholders

Solutions addressing business model, regulatory, healthcare process and IT, medicine

GOAL: MORE EFFECTIVE HEALTHCARE FOR PATIENTS
Philanthropy as a Source for Innovation

Overview of the Pritzker Neuropsychiatric Disorders Research Consortium
Introduction

• Mission
• Background
• Members
• SAB
• Research and Discovery Strategy
• Findings
• Patent and Business Strategy
Mission

• To discover the neurobiological and genetic causes of three major psychiatric disorders
  – Major Depressive Disorder (MDD)
  – Bipolar Disorder (BPD)
  – Schizophrenia

• To identify biomarkers for better diagnosis and novel targets for their treatment

• To ensure application of these discoveries in the development of diagnostic and treatment strategies
Background

• Pritzker funding started in the late 70’s

• The Pritzker *Network*
  - From 1996 to 2000
  - Cornell, Michigan and Stanford
  - Network was interdisciplinary, collaborative and based on established relationships

• The Pritzker *Consortium*
  - Established in 2000 and extended in 2011 for another 5 years
  - Originally Michigan, UC Davis, UC Irvine and Stanford
  - Cornell and HudsonAlpha joined in 2005 and 2008 respectively
  - UCD withdrawn after Dr EG Jones passed away in June 2011.
  - Focus on gene expression, genetics and clinical studies
  - Shared IP policy
Member Institutions & Site Directors

- University of Michigan
  Huda Akil and Stan Watson
- Cornell University
  Jack Barchas
- University of California at Irvine
  Biff Bunney
- HudsonAlpha Institute
  Rick Myers
- Stanford University
  Alan Schatzberg
- University of California at Davis*
  Ted Jones

* UCD withdrawn after Dr. Jones passed away.
Scientific Advisory Board

- **Steven Paul:**
  Director of the Helen & Robert Appel Institute for Alzheimer’s Disease Research at Weill Cornell Medical College. Former EXVP at Lilly

- **Floyd Bloom:**
  Ex-Director at the Scripps Research Institute, former CEO of Neurome

- **David Hamburg:**
  President Emeritus, Carnegie Corp. of NY, now at Weill Medical College

- **Bruce McEwen:**
  Alfred E. Mirsky Professor at Rockefeller University
Scientific Approach

- Multidisciplinary and integrated approach that includes neuroscientists, psychiatrists, geneticists, statisticians and informaticians
- “Circuit Neuromics” approach that requires the integration of genetics, cell and molecular biology, functional neuroanatomy and behavioral and clinical analyses
- Brain Bank from subjects with MDD, BPD, schizophrenia and controls
- Human clinical samples from living, well-diagnosed psychiatric patients and controls
- In depth in animal and in vitro models
Strategies

- Identification of differentially expressed genes and of structural variation via microarrays
- Validation and downstream analysis of array results using alternate technologies
- Sample collection for follow-up studies
- Whole genome association studies and additional Genetic and Genomics sequencing studies
R&D Platform

DISCOVERY PROCESS
- Brain Bank ⇒ microarray ⇒ candidate genes
- Animal disease models ⇒ microarray ⇒ candidate genes
- Isolated population ⇒ linkage disequilibrium ⇒ candidate loci
- DNA samples ⇒ association study ⇒ candidate genes

TARGET VALIDATION/FOLLOW-UP STUDIES
- qRT-PCR
- RNAi
- Western analysis and protein function studies
- Anatomical studies (In Situ Hybridization, 3D)
- Gene function/Promoter regulation
- Genetic and Genomic Sequencing
- Epigenetics: Genome-wide methylation
- Cellular assays
- Animal Behavioral studies (Behavioral/Drug Response/KO)
- Clinical studies
  - Sample collection
  - Imaging

BIOINFORMATICS DATABASE
- Integration
- Data analysis
Discovery Platform Overview

Target Identification
- Brain Bank
- Animal studies
- Genomics

Target Validation

Clinical Characterization of Phenotype
- Imaging
- Sample collection

Bioinformatics

- Genotyping
- SNP ID

Gene Function
- Promoter regulation

Anatomical Studies

Behavioral Drug Response/KO

PCR
- SAGE
- Arrays
Case study of target identification and validation – dysregulation of the FGF system in mood disorders
Dysregulation of the Fibroblast Growth Factor (FGF) system in Mood Disorders

- FGF system – comprised of 22 ligands (10 of which are expressed in brain) and four receptors distinguished by differential ligand affinity and by tissue-specific expression
- The FGF family has been implicated in the regulation of cell differentiation, migration and mitogenesis and in multiple pathological processes, most notably, tumorigenesis and skeletal disorders
- Small molecules and gene therapies targeting the FGF system have advanced into clinical development for cardiovascular and oncology indications
- Consortium scientists were the first to identify dysregulation of the FGF system in mood disorders
Dysregulation of the FGF system in MDD

- Several FGF system transcripts identified to be differentially expressed in frontal cortical regions of MDD subjects – the effect is **specific to MDD** and not seen in BPD
- Results confirmed in an independent cohort and by PCR, *In Situ* hybridization and other array platforms (i.e. Illumina)
Dysregulation of the FGF system by antidepressants

- Array findings not due to antidepressant treatment
- In Rats: FGFR2 expression increased by fluoxetine in hippocampal and frontal cortical regions, a change opposite to that seen in MDD
Non-human primate studies

1) **M. mulatta treated with lithium, olanzapine and haloperidol**
   - Specific genes and pathways are significantly altered by lithium
   - Several of these genes show reciprocal changes in BPD

2) **Squirrel monkeys under social stress paradigm**
   - Animals exposed to repeated cycles of isolation and social stimulation
   - Social isolation induces hypercortisolism
   - Hypercortisolism impairs cognition whereas social stimulation after isolation enhances learning and memory
   - Social stimulation after isolation increases hippocampal neurogenesis. Similar response as seen following antidepressants (ADs) administration
Neuroimaging and Clinical Capabilities and Track Record Across the Consortium

- First rate clinical operations at each of the Consortium Sites with a track record of clinical research (e.g. part of STAR D).
- Human Neuroimaging Capabilities including PET and fMRI.
- Track record of collaborative clinical research under the Pritzker Network, including neuroimaging, neuro-endocrinology and clinical treatment outcome.
- Track record of studies correlating genotyping and neuroimaging responses.
R&D Strategy Overview

Susceptibility Genes & Treatment Targets

ANIMAL STUDIES
- Rodents: Rats Selected Lines
- Mice: Transgenics & KOs
- Non-Human Primates
  Pharmacological Studies
  Behavior, Neuroendocrinology & Genetics

HUMAN STUDIES
- Replication & Extension to New Populations of Subjects & Other Disorders
- Phenotyping in Patient Populations:
  Correlations Between Genetics, Neuroimaging & Other Markers.
  Disease Profile & Treatment Response

Better Targets Biomarkers
Patent Strategy & Committee

- Tasked with ensuring Consortium inventions will be protected and commercialized, preferentially through partnerships with industry

- The Patent Committee is comprised of representatives from Stanford University, Kilpatrick Townsend, members of the Pritzker Fund and the Scientific Liaison
Business Goals

- To develop Consortium IP into a self-sustaining “enterprise” capable of generating continuous funding for ongoing research activities

- To build relationships with companies or outside organizations focused on the CNS space or related fields – ideally with those developing technology that addresses Consortium needs
THANKS

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