

BREAKING OUT of the SILO MENTALITY

**FLYING OVER THE VALLEY OF DEATH:
ACCELERATING from DISCOVERY to PRODUCT**

GUIRR

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DISCLOSURE

- 🦆 Chairman of the Board of Directors of Solace Pharmaceuticals
- 🦆 Senior Fellow at Ewing Marion Kauffman Foundation
- 🦆 Partner of Pure Tech Ventures, Inc.
- 🦆 Scientific Advisor for Bayer Health Care
- 🦆 Former Executive Vice President of Aventis Pharmaceuticals, responsible for global research, development and regulatory
- 🦆 Former faculty member and administrator at MIT.
- 🦆 Former chairman of the Board of Directors of Alantos Pharmaceuticals, Inc.

WHAT DO WE NOT KNOW?

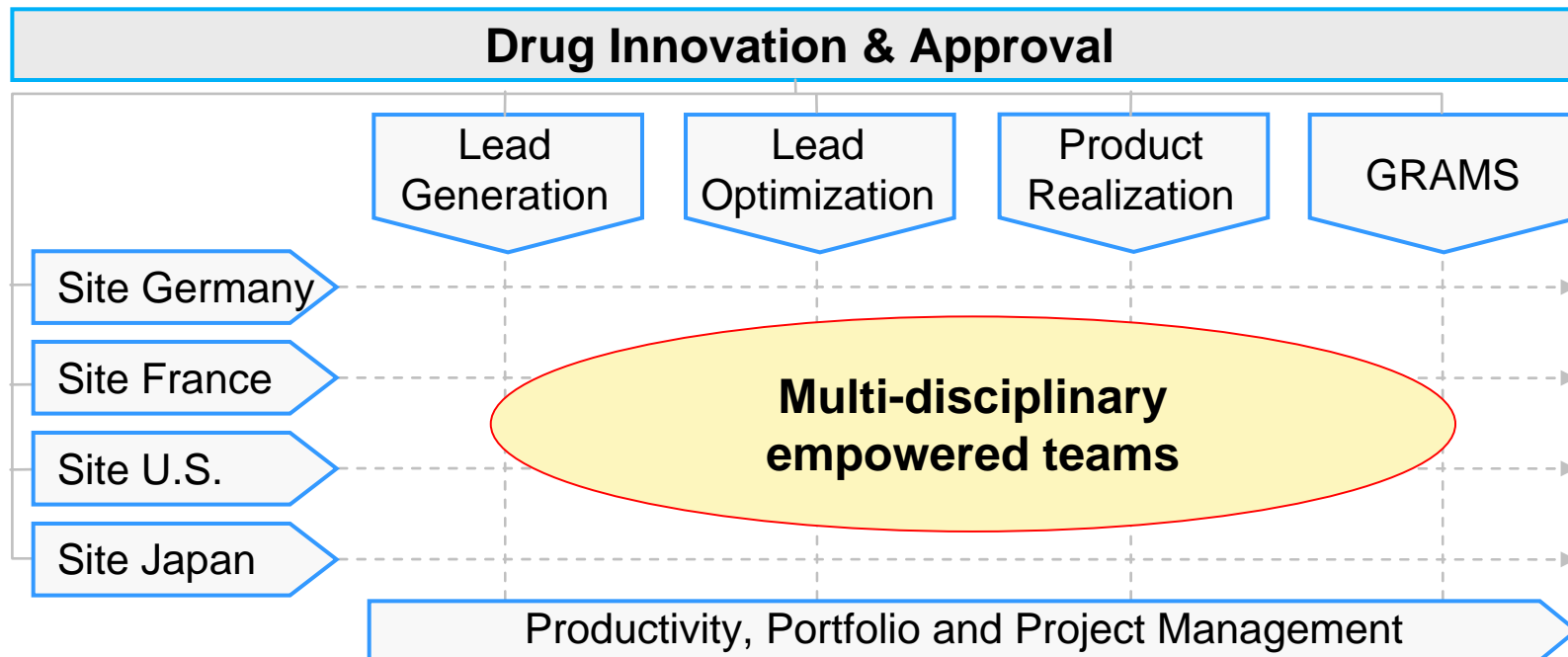
- ✉ Which targets will give the optimal benefit/risk ratio ?
- ✉ Which patients will best respond to which therapy?
- ✉ Which patient will be susceptible to which side effect from which therapy?
- ✉ Which strategy, small molecule or biologic, should be pursued?
- ✉ Which low frequency side effect signal is a ticking time bomb?

WHAT HAVE I LEARNED?

- 👤 Drug Innovation & Approval
- 👤 Chemical Biology
- 👤 Pure Tech Ventures and Solace
- 👤 MIT Center For Biomedical Innovation

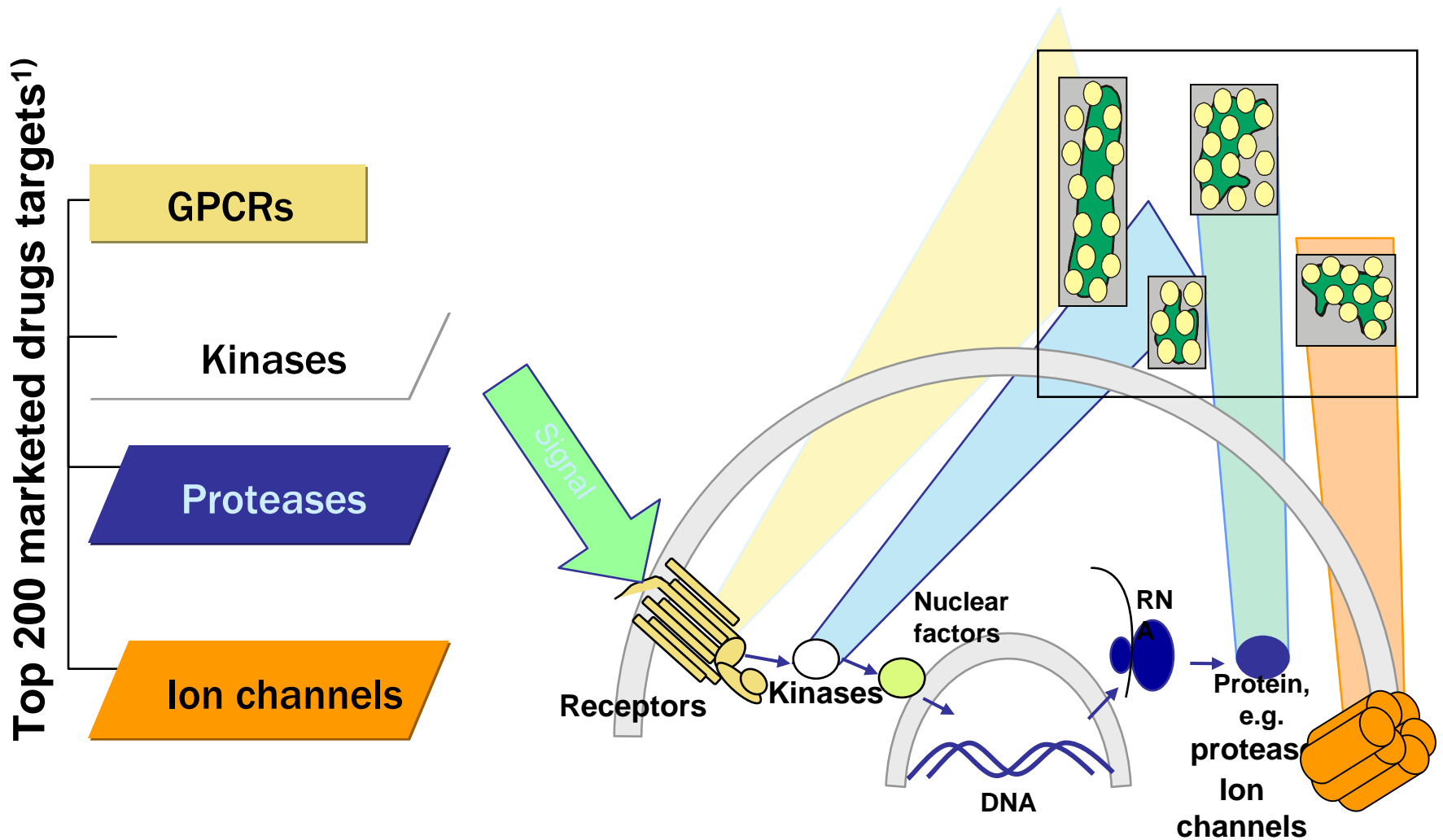
Implementing Drug Innovation & Approval

- Project teams are the units of innovation
- Entrepreneurial sites driving innovation and productivity
- Best-in-class technologies and expertise in global Functions / CoEs



GRAMS = Global regulatory approvals & marketing support

CHEMICAL BIOLOGY - Four Target Family Platforms



CHEMICAL BIOLOGY - Global Platform - KINASE

Discovery team: 250-300



The Chemical Biology Platforms

Matching biological and chemical space

- **Leverage globally the target family knowledge across projects independent of targeted diseases and Sites**
- **Improve Aventis' target family compound collection (focused libraries)**
- **Develop and apply the concept “ all target compounds see all targets of a family”**
- **Develop target family specific predictive models and tools**
- **Use external networks of experts in the field**

 **Better compounds faster**

CHEMICAL BIOLOGY

	Traditional drug discovery	DI&A chemical biology
Targets	<ul style="list-style-type: none">• Collection of targets	<ul style="list-style-type: none">• Selected target families
Workflow	<ul style="list-style-type: none">• Sequential activities in chemistry and biology	<ul style="list-style-type: none">• Simultaneous efforts in internal and external networks
Scientific concept	<ul style="list-style-type: none">• Traditional disciplines	<ul style="list-style-type: none">• Knowledge-based approaches in biology and chemistry
Organization	<ul style="list-style-type: none">• Silos of functionality	<ul style="list-style-type: none">• Cross-functional, beyond disciplines, virtual, capability-oriented, DI&A network-centric
	<ul style="list-style-type: none">• Existing skills in disciplines	<ul style="list-style-type: none">• Best in class, knowledge-based, learning curves
Capabilities	<ul style="list-style-type: none">• Individual projects	<ul style="list-style-type: none">• Focus on optimizing the global target family portfolio
Value	<ul style="list-style-type: none">• Functional, hierarchical lines of command	<ul style="list-style-type: none">• Entrepreneurial, value-oriented
Mind-set	<ul style="list-style-type: none">• Compound Focus	<ul style="list-style-type: none">• Common Mechanism Focus

Source:
CBK

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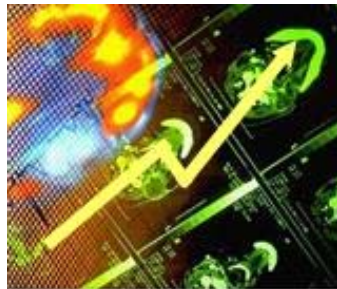
PURETECH'S PROACTIVE MODEL



Identify an Area of Unmet Need
Where Innovation Can Be Translated



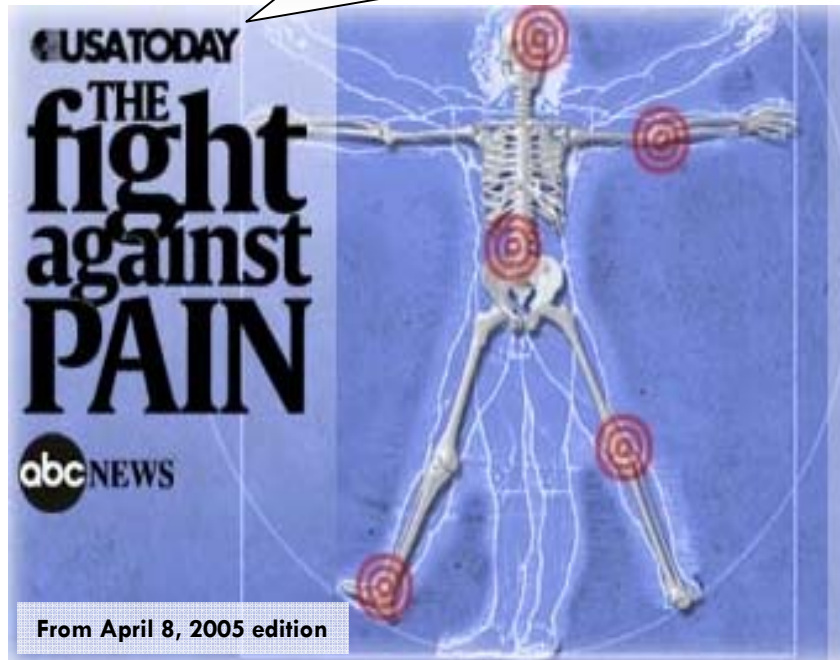
Gather the World's Leading Experts
And Uncover Seminal Technologies



Find & Conduct The Key Experiments
That Will Either Drive Value Or Kill The
Program

LARGE & GROWING MARKET OPPORTUNITY

40 million US adults experience chronic pain



Neuropathic pain is a debilitating subset

- 17 million people in the US
- Diabetic neuropathy, post-herpetic neuralgia, HIV neuropathy, trigeminal neuralgia are primary causes

Current drugs are marginally effective with side effects

Case Study

US neuropathic pain market is \$3.5 B
and growing 10% per annum

SOLACE SCIENTIFIC ADVISORY BOARD

Pain mechanisms

Clifford Woolf, MD, PhD – Prof. and Chair of Anesthesia, Harvard Medical School, MGH; *Solace SAB Chair*



Chronic pain

Allan Basbaum, PhD – Professor and Chair of Anatomy, UCSF



Ion channels

Bruce Bean, PhD – Prof. of Neurobiology, Harvard Med School



Microglia

Joyce DeLeo, PhD - Prof. of Anesthesiology & Pharmacology, Dartmouth Med School



Clinical trials

Roy Freeman, MD- Prof. of Neurology, Harvard Medical School; Director Center for Autonomic and Peripheral Nerve Disorders



Regulatory

Lee Simon, MD –Clinical Medicine, Harvard Med School; former FDA Director, Analgesia Division



Spinal pharmacology

Tony Yaksh, PhD – Prof. of Anesthesiology and Pharmacology, UCSD School of Med



Case
Study

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CORE DEVELOPMENT PROGRAMS



Program 1: SLC022

Existing compound - new link to pain

Compound has been safely administered to 1000's of people

PI discovered the critical role of glia in pain transmission ("hot" new area in pain research)

Compound not previously approved in US/Europe; lacked efficacy in original indication

Exclusive license to enabling intellectual property

Case Study



Program 2: SLC262

Molecule discovered to be key to pain sensitivity

Genetic mutation in ~3% of population linked to reduced pain in humans (November issue of *Nature Medicine*)

Compound mimicking mutation reduces pain in animals

Discovered by thought leader in pain research. PureTech executed license pre-publication

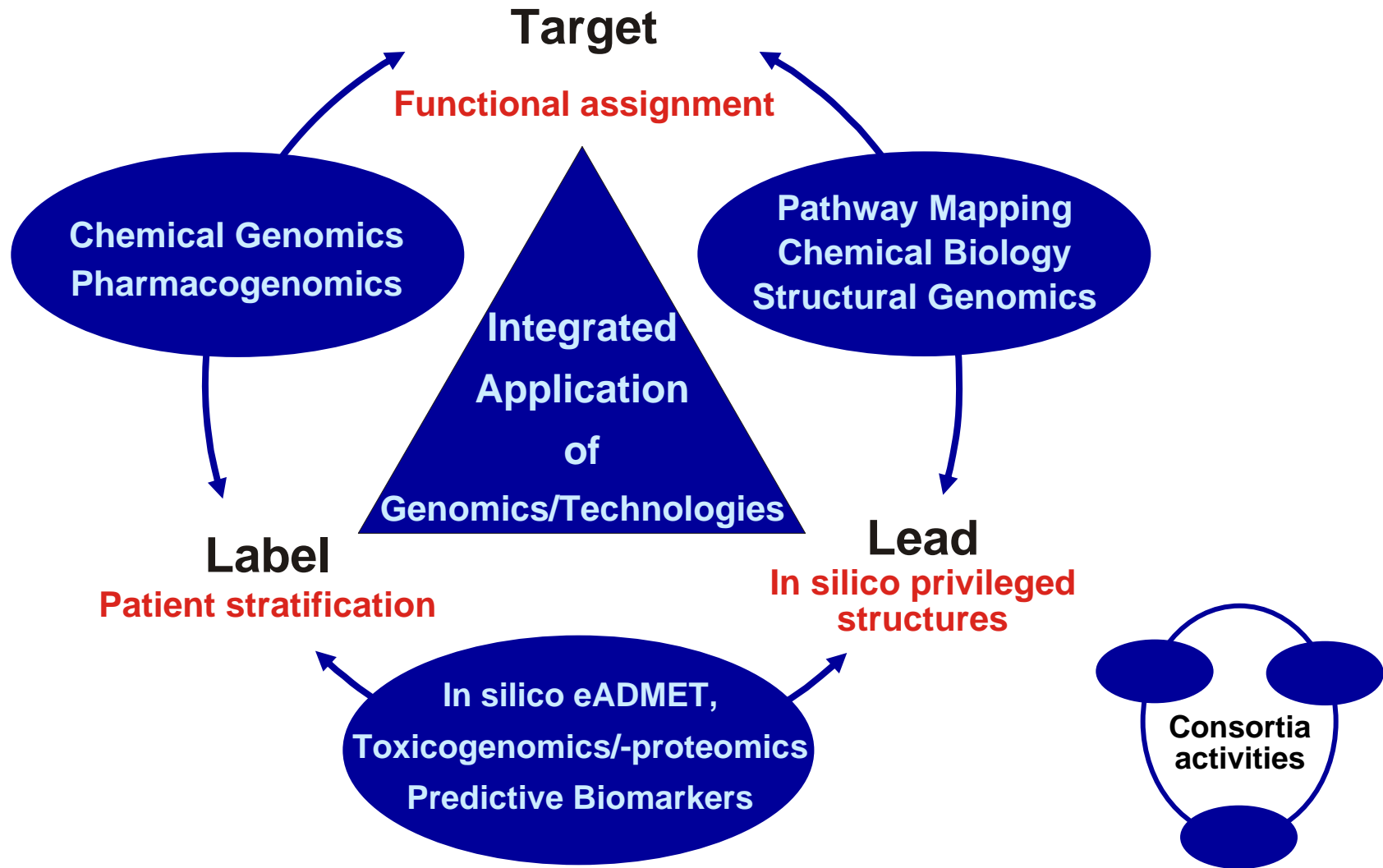
MIT Center for Biomedical Innovation - MISSION

The mission of MIT CBI is to transform the discovery, development, manufacture and distribution of cost-effective therapeutics and devices.

To achieve this, we have created a **'safe haven'** in which academic, government and industry experts collaborate to generate and disseminate high-impact systemic solutions that enhance efficacy, safety, and quality of patient care, worldwide.

Next paradigm in Drug Discovery depends on...

Impact of Genomics on Drug Discovery



BLACK SWAN SCENARII : INTERNAL FORCES

Large Pharma will focus on:

- 🦢 Strategic Discovery Clusters
- 🦢 New Role for the Alliance Manager
- 🦢 Commercial / R&D spend: 2:1 → 1:1
- 🦢 Approvals after Ph 2b
- 🦢 A changed IP space
- 🦢 Safe Haven and Pre-competitive Space

BLACK SWAN SCENARIO: EXTERNAL FORCES

- Research on few conditions, e.g. Alzheimers, some cancers, orphan diseases
- Mandatory use of generics by drug class
- Identification of responders to efficacy and side effects required for approval and marketing of all non-generics
- Preventive Health measures are preferentially reimbursed
- Price Controls!!!

BLACK SWAN SCENARIO FOR BIOPHARM

- 🦢 3-4 top Tier Large Pharma as integrators
- 🦢 Many small specialty players
- 🦢 Venture Capital Firms as research translators
- 🦢 Virtuality becomes a Reality
- 🦢 Strategic Global Sourcing
- 🦢 Academia/Government/Industry collaborations

BLACK SWAN PILOT FOR BIOPHARM

- Manhattan / Man to Moon style Cancer Project
- Massachusetts state-wide
- Mechanistic pre-clinical and clinical studies
- Methods and Tools for Predictive Power
- Monitoring and Measurement techniques
- Managed Academia/Government/Industry collaborations

BLACK SWAN PILOT FOR BIOPHARM

 WOLLEN KOENNEN MACHEN

 VISION CAPABILITIES IMPLEMENTATION

 JUST DO IT!!!!