

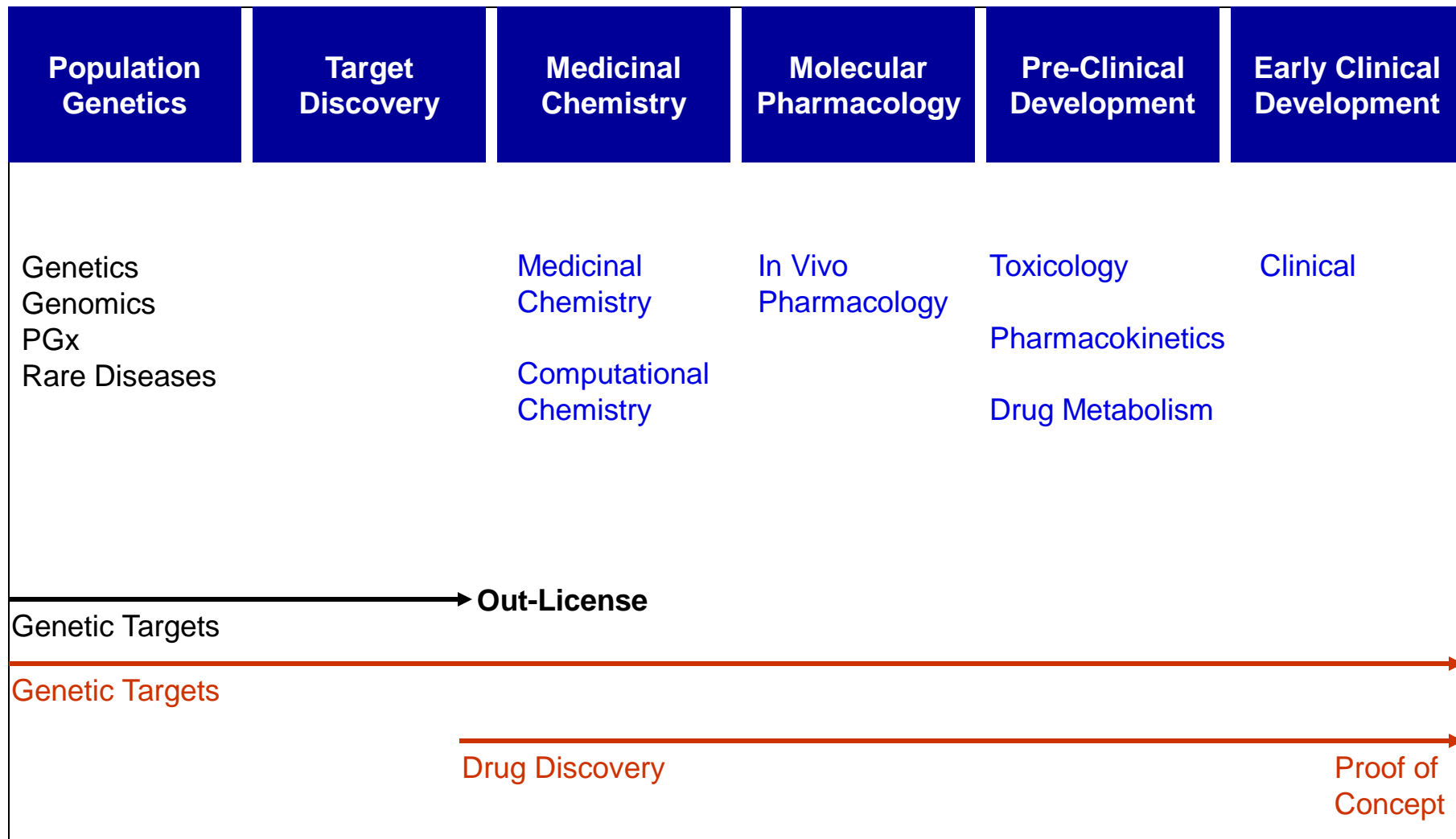


# motif

A discovery engine for the pharmaceutical industry



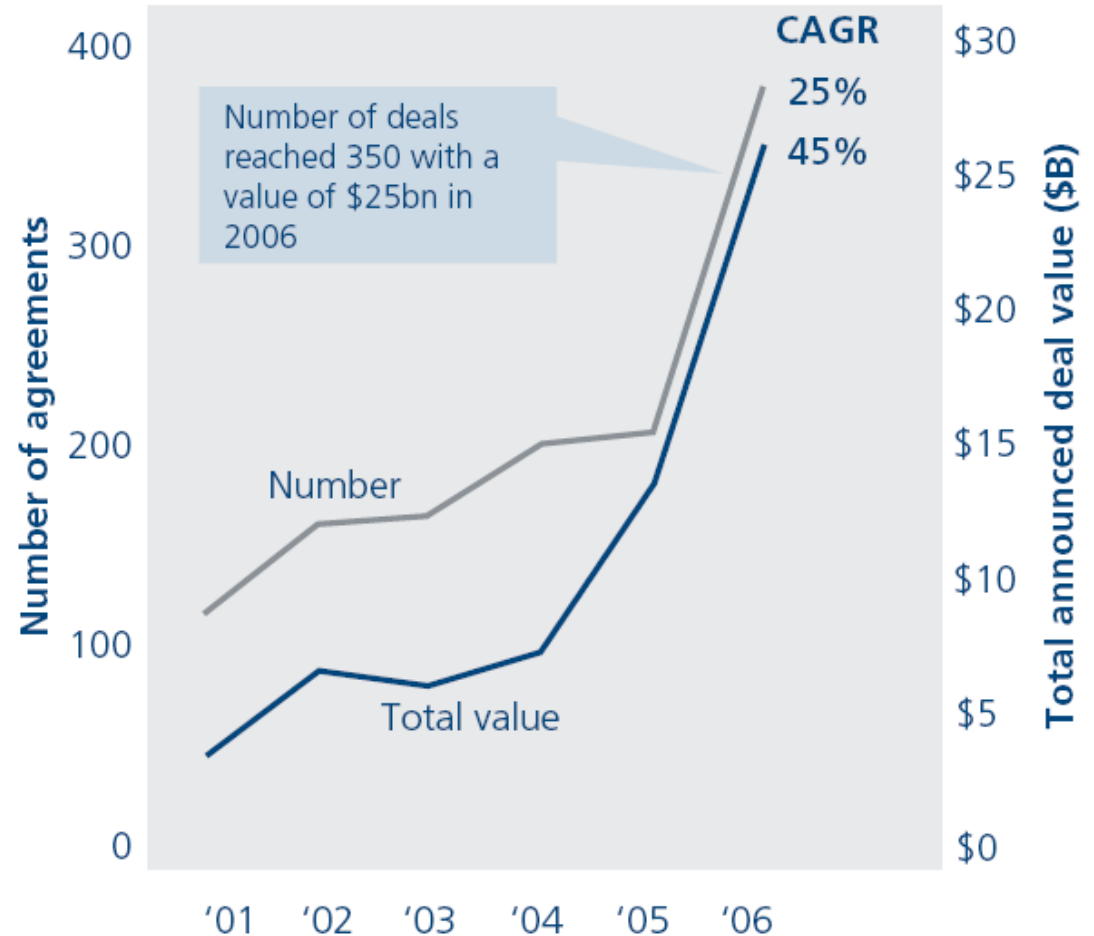
# An integrated discovery continuum



# Radical shift in pharma discovery model

Increasing reliance on in-licensing to provide pharma pipeline – due to lack of success from pharma R&D

- ‘Between 1998 and 2007 the £3 billion spent on research each year delivered no new molecular entities to the market’ (A. Witty CEO, GSK, Feb ‘10)
- Cost of developing successful medicine: \$1.3B over 13 yrs. (PhRMA)



Oliver Wyman, 2009, latest available.

# Current landscape: opportunities for new players

- 50% of new medicinal entities approved in US since 2004 came from small pharma or biotech companies\*
- 65% of new US drugs approved in 2006/7 originated from biotech\*\*
- \$17M upfront valuation of IND ready compounds in 2006\*\*\*
- \$70M upfront valuation of Phase II compounds

\* Munos, *Nature Reviews*, Vol. 8, 2009; \*\* Czerepak & Ryser, *Nature Reviews*, Vol. 7, 2008

\*\*\* Oliver Wyman, 2009, latest available

# The “A” Team from Big Pharma

## Top Company Experience

**Merck, Schering Plough, Wyeth, GSK, Bayer**

### Drug Discovery

John Amatruda M.D

James N. Livingston Ph.D

### Drug Metabolism & Pharmacokinetics:

Gerald T. Miwa, Ph.D: 32 yrs

Biology: James N. Livingston Ph.D: 17 yrs

Clinical: John M. Amatruda, M.D: 17 yrs

Computational Chemistry: Simon K. Kearsley Ph.D: 20 yrs

Intellectual Property: P.S. Kalyanaraman JD, PhD 20 years

### Medicinal Chemistry

Malcolm MacCoss, Ph.D., FRSC: 28 yrs

Matthew J. Wyvratt, Ph.D: 32 yrs

Mark L. Greenlee, Ph.D: 26 yrs

Jerauld S. Skotnicki, Ph.D: 30 yrs

Pharmacology: Euan McIntyre: 24 yrs

Toxicology: James S. MacDonald, Ph.D: 31 yrs

# A stellar drug discovery track record

- US patents issued: 246
- Pre-clinical candidates: > 210 novel small molecules & peptides
- Clinical drug candidates: Type 1 & 2 diabetes, hepatitis C, CINV, COPD, cystic fibrosis, hypertension, heart failure, obesity, cancer



**\$5.6bn**



**\$2.3bn**



**\$1.9bn**



**Prinivil  
\$1.7bn**



**\$1.3bn**



**\$3.6bn**



**\$0.3bn**



**\$2.1bn**



**\$2.2bn**



**\$1.2bn**

Registered trademarks & logos of respective companies

# A world class team

## Management Team

**Richard C.E. Morgan:** Chairman, Co-founder & director, Celgene (cap value: \$23 bn)

**Zaki Hosny:** CEO, 35 years at Merck & Co.

## Board of Directors:

Dr. Mary Lake Polan

Dr. John W. Stakes III

Jonathan E. Gold

Bruce A. Williams

Gerard Moufflet

## Scientific Advisory Board

Jay Tischfield (Chair)

Linda Brzustowicz

Tara Matisse

Ray White

Morris Birnbaum

John Rice

Howard Edenberg



# Lead hopping: launching pad in drug discovery

## Big pharma

Target discovery/validation  
Assay development  
High throughput screening  
In vitro/ In vivo assays  
Lead optimization  
Pre-clinical development  
POC in man



Validated target ?  
POC in man?  
Tractable chemistry?  
Potential clinical differentiation?  
IP freedom to operate?

Develop optimal structure for Best in Class compound



Multiple analog development ↔ biology assays



Pre-clinical development: toxicology; PKDM, in vivo pharmacology

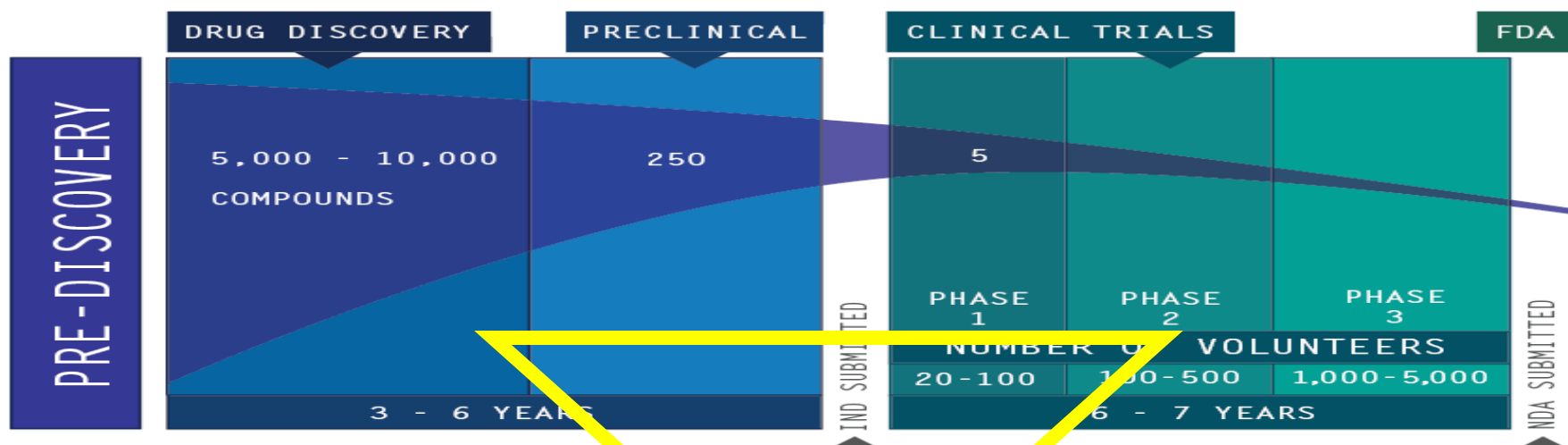


POC in man



License out Best in Class NCE with POC in Man to Pharma after Phase IB/IIA

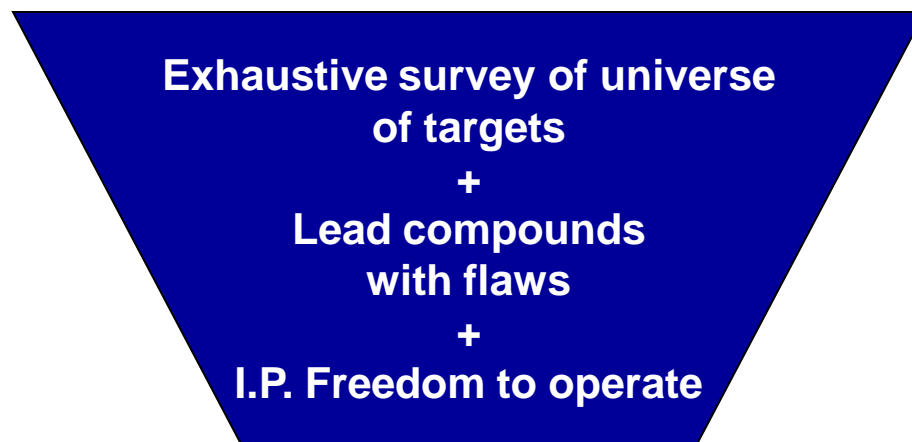
# Lead hopping: the sweet spot in drug discovery



- Lead hopping & optimization from pharma IP
- Develop customized best in class pre-clinical candidates & file IP.
- Pre-clinical development: animal toxicology & pharmacology; formulation development
- Phase I A: IND for first in man studies : acute safety profile; dosage spectrum incl. maximum tolerated dose
- Phase 1 B / II A : Proof of efficacy, safety & optimum dosage in patients

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# Best in Class - New Drug Candidates



Projects	Validated Target	POC in Man	Tractable Chemistry	Clinical Differentiation	I.P. Freedom
MTF 001 / Obesity	✓	✓	✓	✓	✓
MTF 002 / MRSA	✓	✓	✓	✓	✓
MTF 003 / Migraine	✓	✓	✓	✓	✓
MTF 004 / Over Active Bladder	✓	✓	✓	✓	✓
MTF 005 / Rheumatoid Arthritis	✓	✓	✓	✓	✓

# First in class to best in class: a validated model



STATINS: Lovastatin: Atorvastatin

- Improved human pharmacokinetic profile. Greater efficacy & dosage convenience



ACE INHIBITORS: Captopril: Enalapril / Lisinopril

- Structurally- based adverse effects minimized. Improved pharmacokinetics; Once daily dosing



CA CHANNEL BLOCKERS: Nifedipine: Amlodipine

- Improved pharmacokinetic profile. Improved safety & tolerability



AZOLES: Myconazole: Voriconazole

- Non-orally available to oral



ARBs: Losartan: Valsartan

- Improved pharmacokinetic profile.



QUINALONES: Norfloxacin: Ciprofloxacin

- Limited tissue penetration. Systemic penetration

# Leverage outsourcing to reduce burn

- Medicinal chemistry, biology, pharmacology, toxicology, pharmacokinetics/ drug metabolism out-sourced to specialist companies in Asia & Eastern Europe
- Operational flexibility across & within projects
- Minimize fixed costs
- 4 projects simultaneously plus pipeline
- 8-10 scientists per project

# Dynamic Discovery Process

## MOTIF

Define biological activity & liabilities of FIC compound

Define optimal structure of BIC compound

Select & refine analogs

Select analogs for biological assays of target engagement / modulation

Select & refine analogs

## DISCOVERY PARTNER

Develop chemical analogs per spec

Iterate chemical analogs

Conduct biological assays

Iterate chemical analogs

- Highly iterative process: 40 analogs / month / project
- Optimized structure: File IP

Define toxicology, PK, drug metabolism, pre IND

File IND application

Define Proof of concept study

Conduct studies

Conduct studies

POC

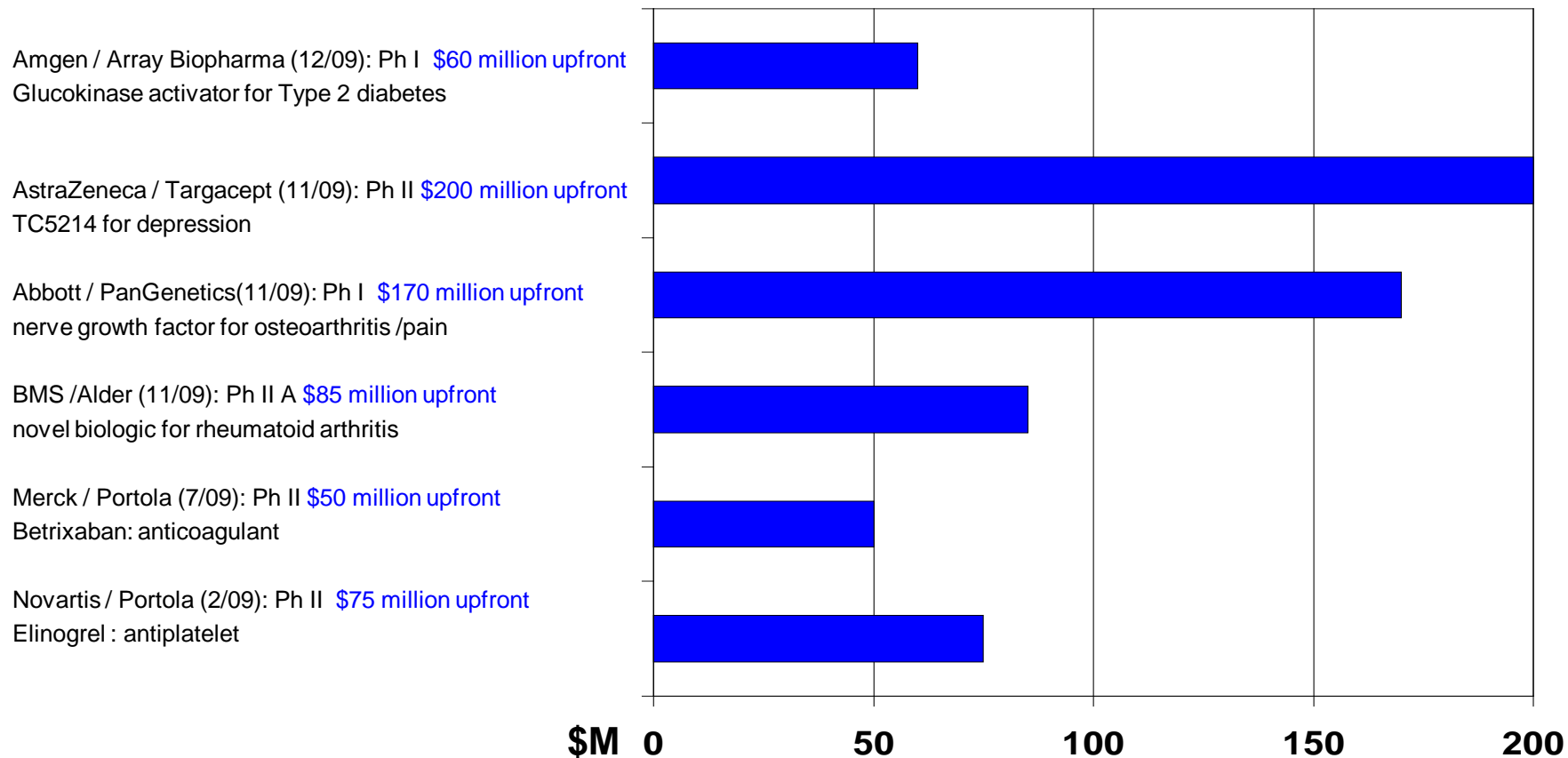
# A progressive model: funding, IP, assets

Months		18	36	48
Projects	Biology/Chemistry	Pre-Clinical / IND	Clinical/POC	
MTF 001		P	IND	
MTF 002				
MTF 003		P	IND	POC
MTF 004		P	IND	POC

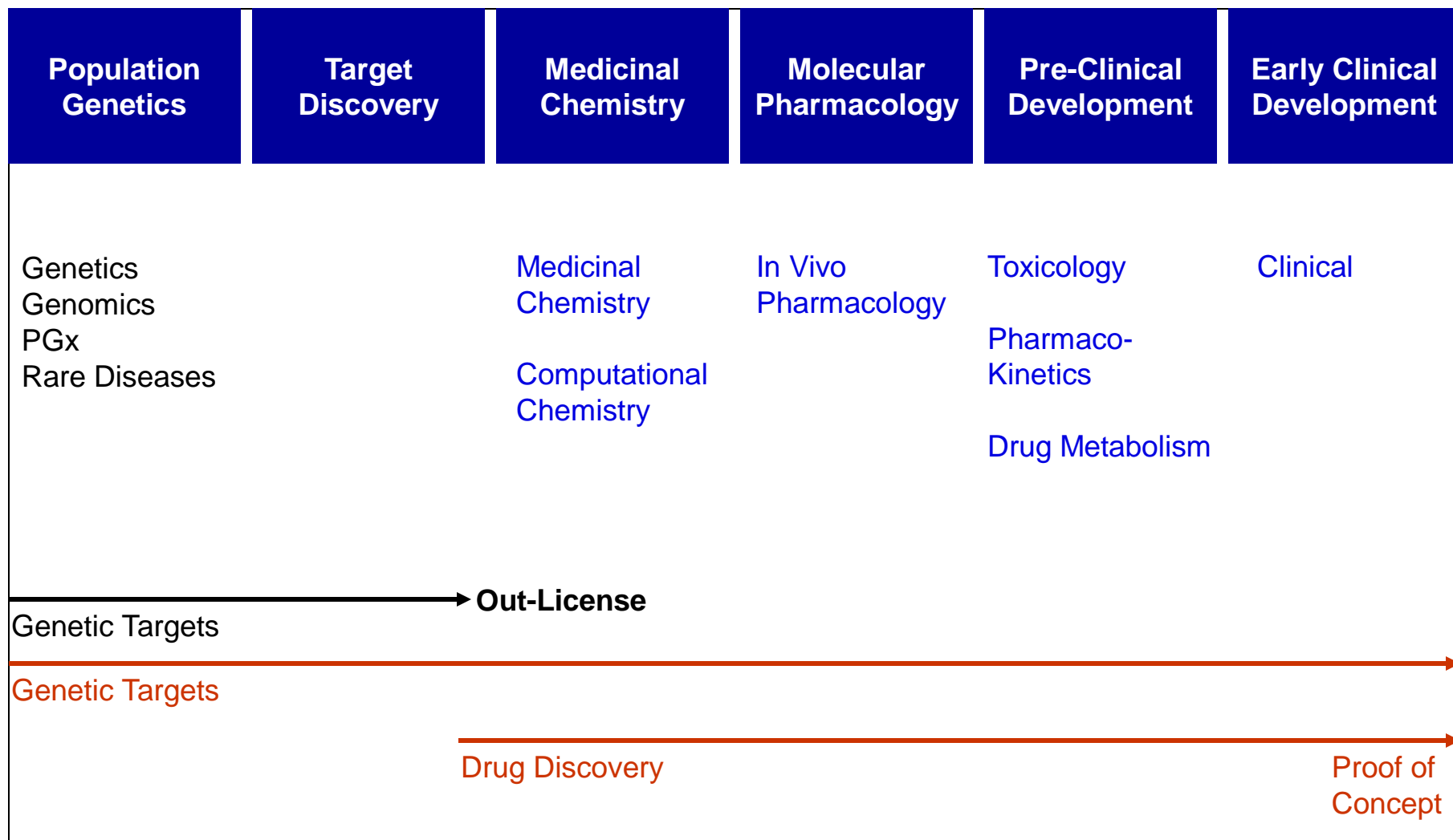
MTF 005		P	IND	POC
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P Patent App & PCC   
 IND Investigational new drug application   
 POC Proof of concept

# Average upfront value of POC deals: \$70-75M



# An integrated discovery continuum



# Value creation: proven foundations

- Proven track record of team in drug discovery & lead hopping
- Proven targets & mechanisms: no speculative projects
- First in class drugs with KNOWN profiles: best in class compounds with meaningful improvement
- Rigorous selection criteria boost probability of success within & across projects

# Value creation: flexible value realization

- Dynamic research process: rapid accumulation of company assets from start
- Proprietary insights, data, discoveries, trade secrets, patents
- Multiple proof points & opportunities to monetize assets: licensing, co-development, intellectual property, IND approvals, proof of concept

# Value creation: validated and benchmarked

- Pharmaceutical companies' licensing-in needs: real and growing
- Best in class vs. first in class: validated across multiple classes
- Develop compounds to proof of concept and license out

# A discovery engine for pharmaceutical industry

- Integrated discovery engine: novel genetic targets, diagnostic biomarkers, drug targets, best in class drugs
- Lead hopping: minimizes risk & expense; maximizes value
- Proven targets, mechanisms, drugs
- Pharma A team with stellar track record
- Small company culture, big pharma discipline



motif

A discovery engine for the pharmaceutical industry

