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BIOSCIENCE PARTNERS

ASENT 11th ANNUAL MEETING

Financing the Neuroscience Pipeline From a VC Perspective

Jonathan J. Fleming
Oxford Bioscience Partners
March 5, 2009

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What I Will Cover

- **Overview of Oxford**
- **The Venture Capital Firm business model**
- **Challenges to the model**
- **The experience in neuroscience**
- **Two examples**
- **What happens in the future?**

Oxford Bioscience Partners

- Leader and innovator in life science venture capital
- Based in Boston, MA
- Five funds totaling $1B of committed capital
- Team of 6 partners, 2 senior advisors, and….
- Executives-In-Residence group with deep domain knowledge and operating backgrounds
- Invest worldwide
- Invest at all stages from seed to public
- Focus on therapeutics, medical devices, diagnostics, research tools and breakthrough bio
- Recent successes include: Sirna, Solexa, Alantos, Powdermed, Hypnion

Oxford Affiliates

OBP Family: Executives-in-Residence

Left to Right: David Armistead, Robert Kamen, David Poorvin, Axel Unterbeck, Manuel Navia

Oded Ben-Joseph

Michael Pavia

Steve Targum

MediQuint

Goal: Identify or create major investment opportunities in Urology

Coordinator: Mike Magliochetti, Ph.D.

- **CEO of Claros Diagnostics**
- **Former Oxford Bioscience Entrepreneur-in-Residence**
- **Former CEO of Hema Metrics and Urosurge**

Clinical Staff:

PETER SCARDINO – Chair of Urology/Chief of Surgery Sloan Kettering, NY
E. DARRACOTT VAUGHAN – Cornell Medical Center and ex chairman AUA
ALAN WEIN – Chief of Urology, Univ. Penn., ex Chairman AUA
STEVE DRETLER – Mass. General Hospital
GEORG BARTSCH – Chair of Urology University of Innsbruck Hospital and Medical Center, Austria

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Accelerated Technologies INCORPORATED

New partnership model for the creation and acceleration of cardiovascular devices into the market.

- ATI was co-founded by Oxford to align the interests of venture capital, key physicians (clinical brain trust) and experienced industry management to accelerate the development, clinical acceptance and commercialization of medical devices into the world market.
- Focused exclusively on Interventional cardiology. Specifically shifting procedures from surgery to the cardiac catheterization lab.
- Contractual relationships with recognized thought leaders.
- Pathway Medical (an OBP V investment) came directly out of ATI.

GREGG STONE, M.D. – Columbia University Medical Center
DANIEL BURKHOFF, M.D., Ph.D. – J. Skirball Center for Cardiovascular Research
EBERHARD GRUBE, M.D. – Siegburg Heart Center
MARTIN LEON, M.D. – Columbia University Medical Center/Cardiovascular Research Foundation)
PAUL TEIRSTEIN, M.D. – Scripps Clinic
BARRY T. KATZEN M.D. - Founder and Medical Director of Baptist Cardiac & Vascular Institute
JEFF MOSES, M.D. – Columbia University Medical Center

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Oxford's Neuroscience Portfolio

- Synaptic
- Memory
- Hypnion
- Psychiatric Genomics
- Acadia
- Targacept
- Descartes
- BrainCells
- Exonhit
- Predix

Almost entirely focused on mental illness and Alzheimer's

Almost entirely focused on symptomatic relief, not disease modification

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VC Business Model: The X Fund

Assumptions for X-Fund

- $100 million Fund
- 20 investments at $5 million per investment

4	return	0		
2	return	investment	or	$10
3	return	2X	or	$30
3	return	3X	or	$45
3	return	4X	or	$60
2	return	5X	or	$50
1	returns	6X	or	$30
1	returns	7X	or	$35
1	returns	8X	or	$40
20				$300 million

15% of deals produce 1/3 return

40% of deals produce 70% return

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VC Business Model

- **Until 2000, most VC backed companies went public on the stock market.**
- **At the time of going public, the investors should own about 75% of the company with the remainder split between founders, managers and science /clinical advisors.**
- **If $75 million went into the company prior to an IPO, then the company should be worth $100 million prior to its IPO.**
- **If the public company is worth $500 million after it begins trading, then the VC investor will have made five times their money.**
- **To make a higher multiple, the company will either have to be worth more, or less capital will have to be put into the company prior to the IPO.**
- **What happens when more than $75 million is put into the company prior to the IPO?**

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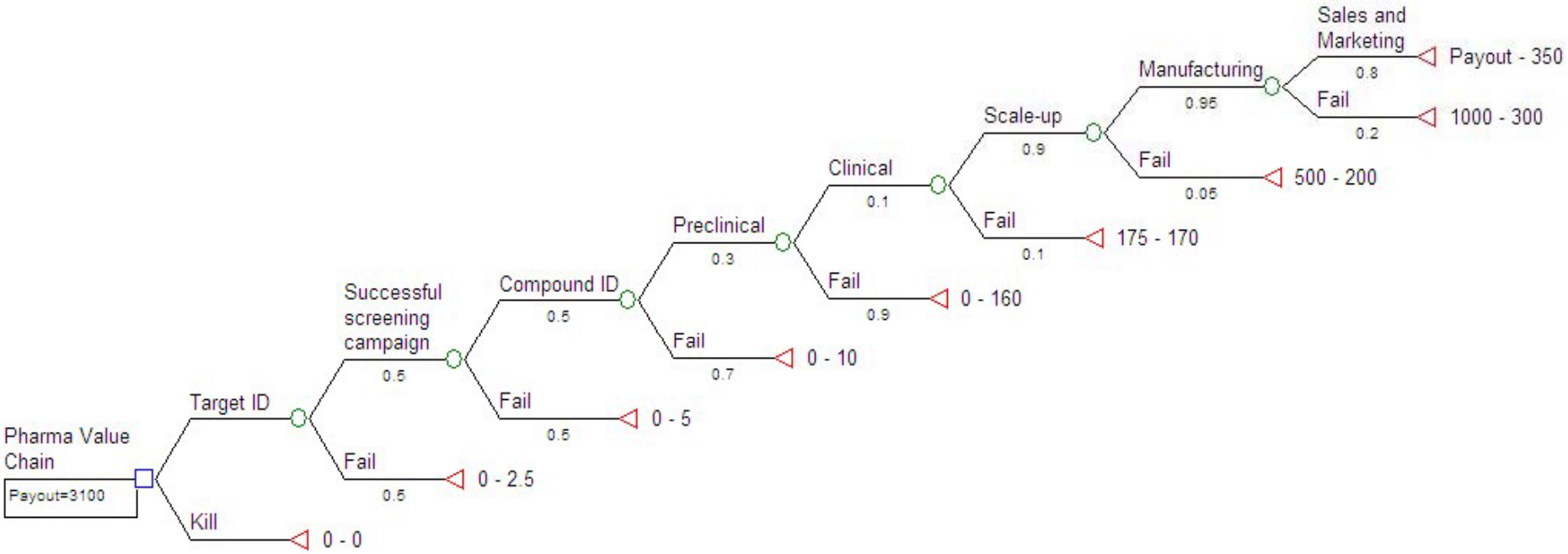
Why is the VC Business Model for Life Science Companies Difficult to Succeed In?

- Competitive advantage is based on proprietary technology; the power to exclude is the source of profit
- Intellectual property can have enormous value, however….
- However, IP is very, very difficult to value
- IP has different values to different parties at different times; the founder often sees it differently than the VC or the corporation
- When is IP worth a lot and when is it worth nothing?


Pharma Value Chain
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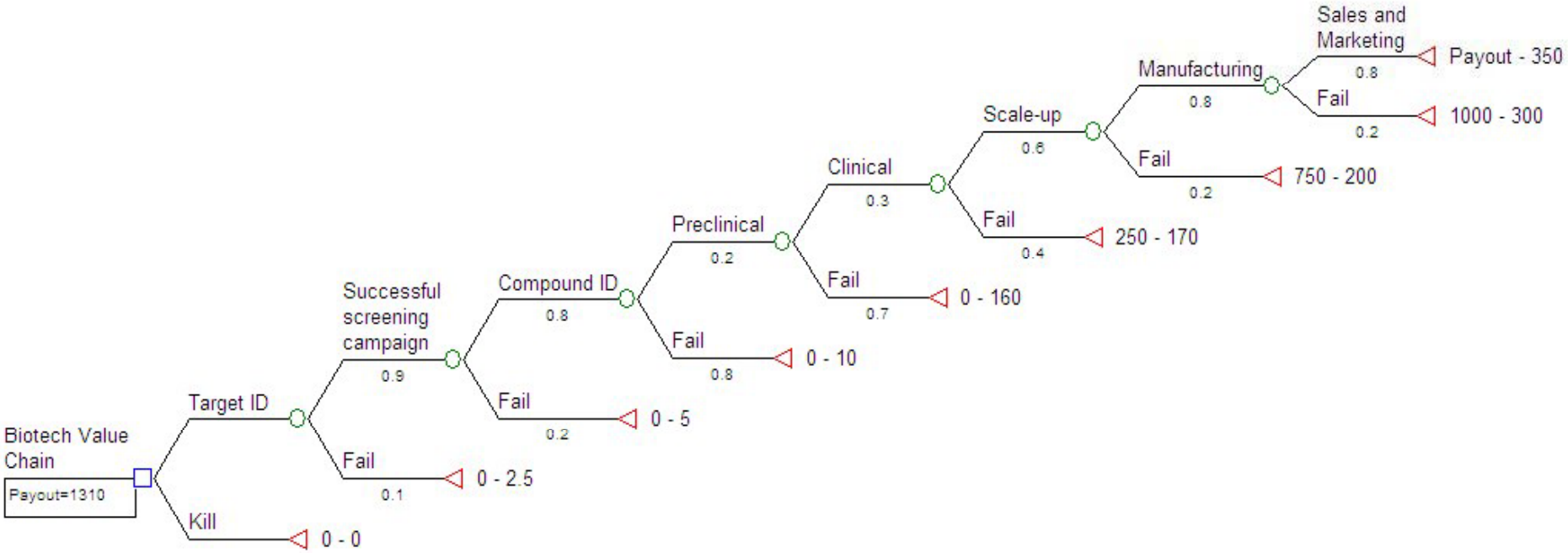
Target ID
Kill
0 - 0
Successful screening campaign
0.5
Fail
0.5
0 - 2.5
Compound ID
0.5
Fail
0.5
0 - 5
Preclinical
0.3
Fail
0.7
0 - 10
Clinical
0.1
Fail
0.9
0 - 160
Scale-up
0.9
Fail
0.1
175 - 170
Manufacturing
0.95
Fail
0.05
500 - 200
Sales and Marketing
0.8
Payout - 350
Fail
0.2
1000 - 300


Biotech Value Chain
Payout=1310
Target ID
Kill
0 - 0
Successful screening campaign
0.9
Fail
0.1
0 - 2.5
Compound ID
0.8
Fail
0.2
0 - 5
Preclinical
0.2
Fail
0.8
0 - 10
Clinical
0.3
Fail
0.7
0 - 160
Scale-up
0.6
Fail
0.4
250 - 170
Manufacturing
0.8
Fail
0.2
750 - 200
Sales and Marketing
0.8
Payout - 350
Fail
0.2
1000 - 300

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Why is the VC Business Model for Life Science Companies Difficult to Succeed In?

The role of risk and uncertainty is much greater in life science companies.

There is tremendous uncertainty in estimating the probability of success of product development at many different steps in the process.

Some of this risk is clinical risk and some of this is regulatory risk.

Worse - Success or failure is often binary!!!

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Why is the VC Business Model for Life Science Companies Difficult to Succeed In?

- The second uncertainty is estimating the value of the enterprise once a particular milestone has been achieved.
- These assets are usually sold based on the value of their future potential instead of a multiple of current revenues
- There are many methods to determine future value
- The estimates of future value depend upon the likelihood of success in getting all the way to the market and having a successful product.

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VC Biotech Business Model

- **Biotechnology promised to increase certainty of success, reduce risk, shorten time and reduce capital requirements of success of novel pharmaceutical development**

- **This lead to the rise of the biotech IPO window every few years when another new wave of technology promised to achieve what the previous wave had not accomplished to date.**

- **Over 340 public biotech companies by 2000**

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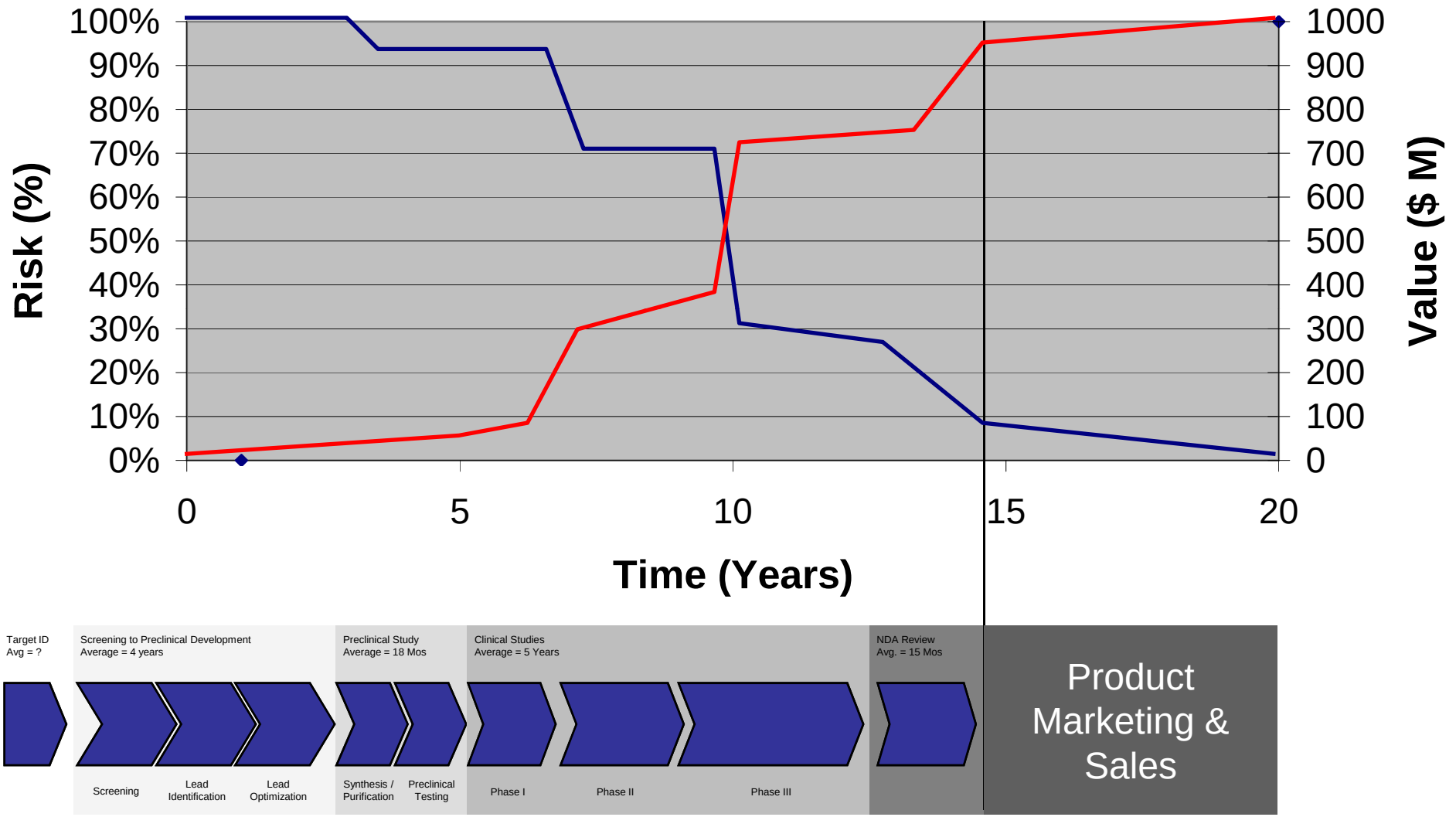
Pharmaceutical Value Chain



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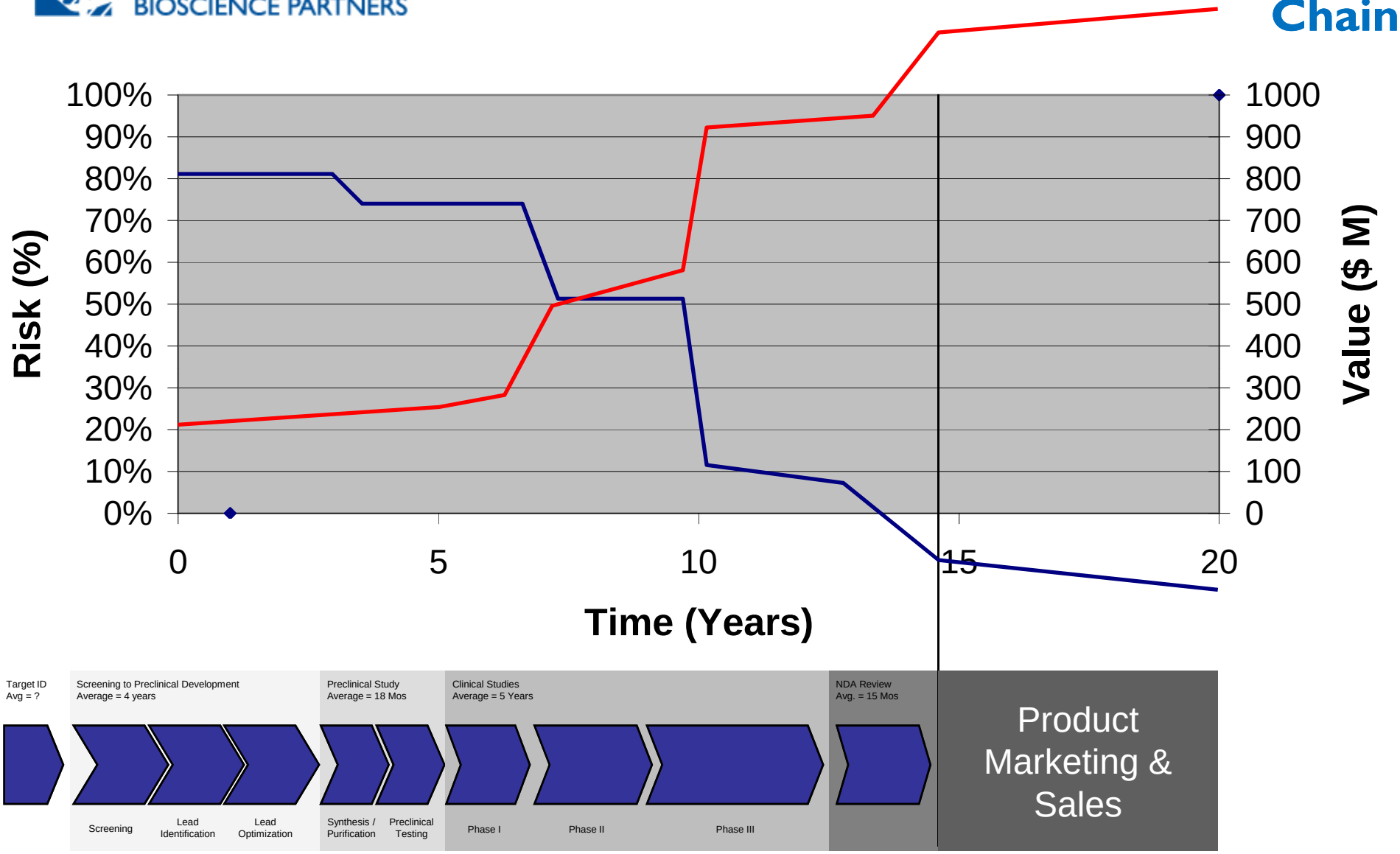
Biotech Promised to Change the Value Chain



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The Rise of the Biotech IPO

Year	#IPOs	Cum IPOs	Ave first day value
1980	2	2	162
1981	8	10	162
1982	5	15	164
1983	24	39	165
1984	3	42	166
1985	3	45	166
1986	21	66	169
1987	10	76	171
1988	3	79	175
1989	3	82	173
1990	5	87	177
1991	30	117	182
1992	32	149	190
1993	22	171	196
1994	21	192	196
1995	22	214	220
1996	39	253	244
1997	21	274	277
1998	9	283	274
1999	11	294	336
2000	48	342	611

Biotech IPO Valuation:
R&D, Human Capital Quality,
And Underwriter Education
Kuntara Pukthuanthong*
San Diego State University

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The Model Does Not Work - The Risks and Uncertainties Are Higher Than Believed

- **Clinical failures**
- **Increase in safety concerns**
- **Increase in FDA uncertainty**
- **Increase in competition**
- **Rational pricing**

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Broken Business Model

- It is clear that the burn rates of biotechs - often millions per month - are not creating value as fast as they are burning it. The business model is broken.

- The easiest way to see this was the change in pricing for the new issue market. The 2004 to 2006 market demonstrated that there were few buyers – they would only pay a fraction above VC cost or later only invest at a discount - $7 special.

- After the Fall of 2007, there have been no biotech IPOs whatsoever

- The value of the current public biotechs that were not profitable lost approximately 75 % of their value in the last 12 months

- The only buyer – the only exit available for investors - is to sell to Big Pharma – they value companies differently than the public equity markets

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New Model

- **Build to sell**
- **Finance only what buyer will pay for**
  - **Innovation validated by a POC trial**
- **Seek to reduce risk and capital requirements**
  - **Safety risk**
  - **FDA risk**
  - **Clinical design risk**
  - **Commercial risk**

Once the public markets stop paying them for starting new companies in this area, entrepreneurs and investors move later in the development pipeline to mitigate the risks and capital requirements of early stage investing.

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Oxford Strategy in Neuro

- **Novelty with impact**
- **Use innovation to increase chances of clinical and commercial success in specific disorders**
- **Be realistic about what a little company can do**
- **Reduce capital requirements to POC**
- **Work closely with disease foundations , FDA and pharmaceutical industry**

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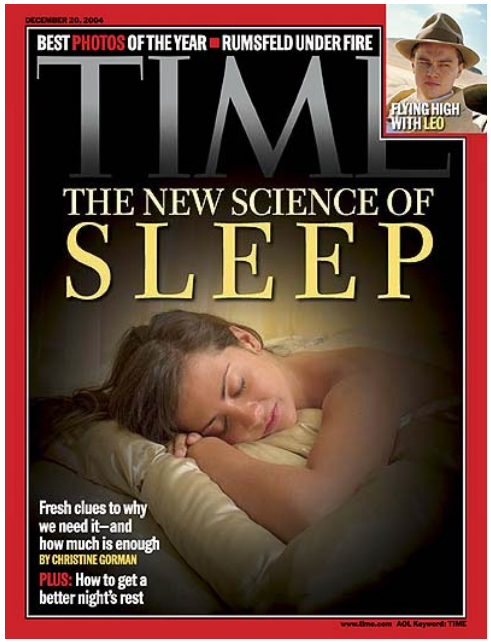
Hypnion

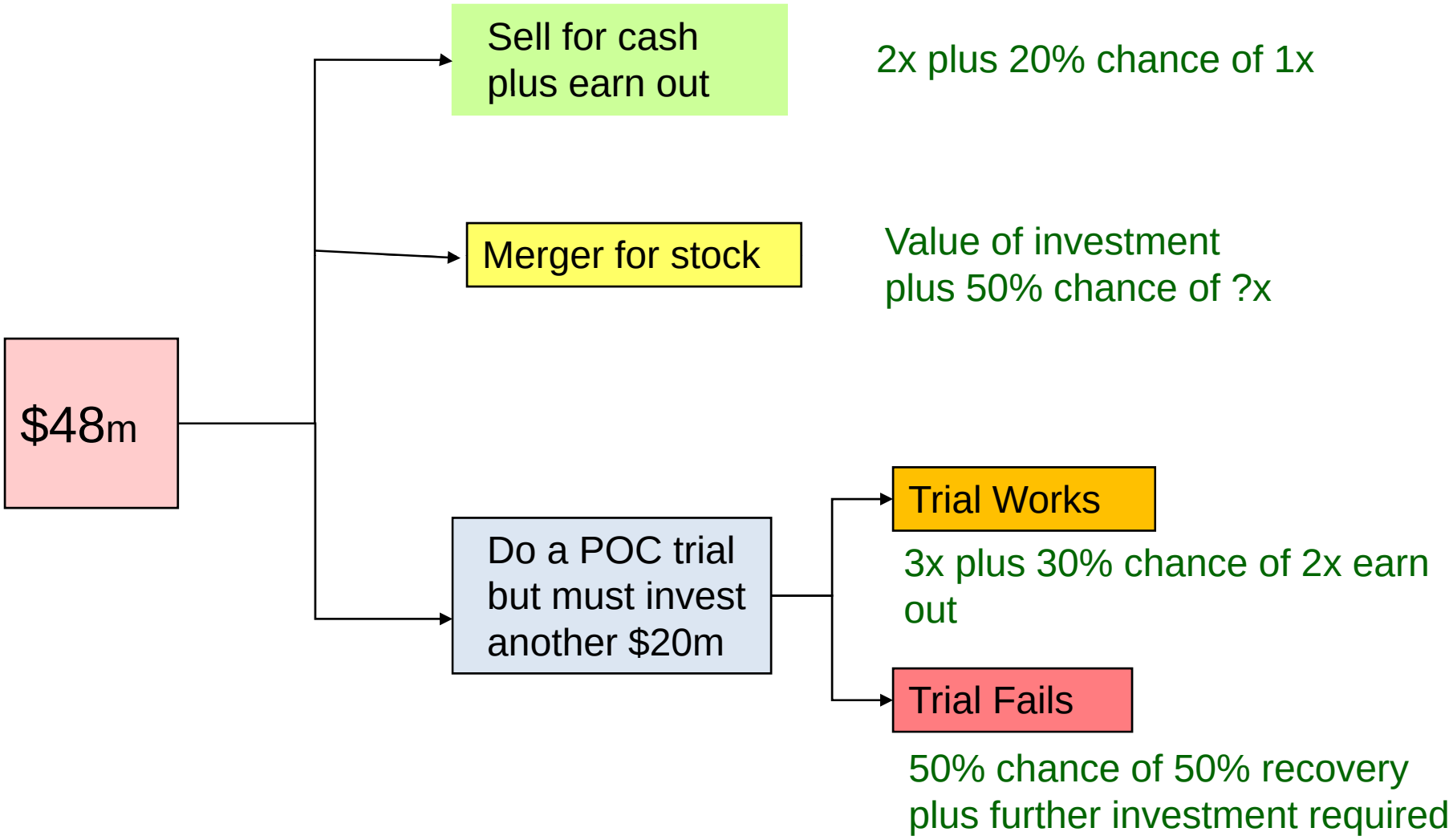
- 1999 Founded out of Stanford, Brandeis, Newton Chili Party
- 2000 Oxford leads Series A round
- 2003 First Hypnion compound enters clinic
- 2005 HYP 10275 – first enters clinic
- 2007 Sold to Eli Lilly for $315

SCORE system enabled almost perfect prediction of efficacy in insomnia as well as comparative data to current products

Did not predict safety and PK/PD!



The Double Uncertainty of Outcome and Value of Outcome Even if Efficacy is Predictable



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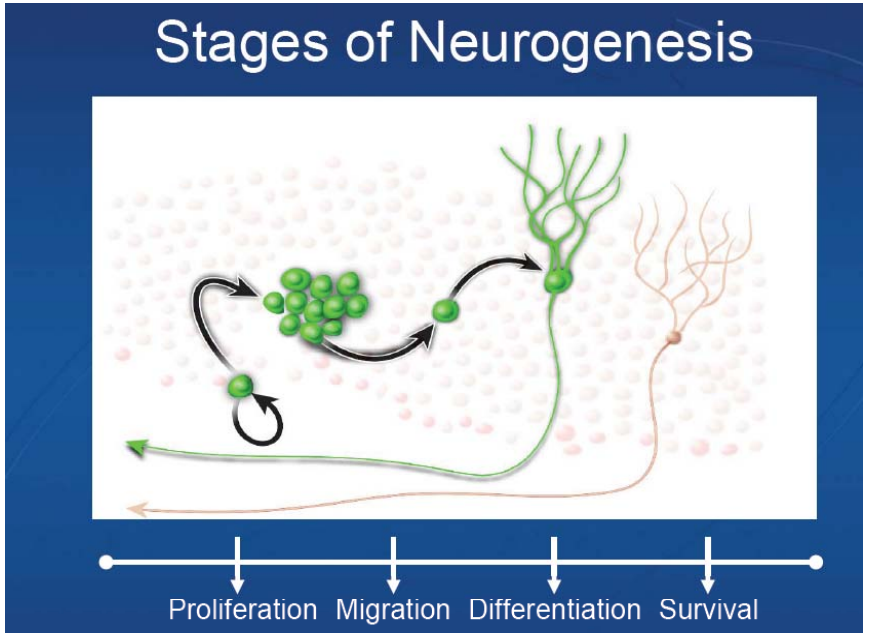
BRAINCELLS

- **Oxford founding investor**
- **Breakthrough science: Neurogenesis**
- **Use stem cells as screens to identify compounds that drive proliferation but also correct and complete differentiation into functioning neurons**



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Future

- Oxford has not made a new neuro investment in 6 years
- Unlikely to make one in the foreseeable future
- The difficulty, risk and uncertainty of getting to a point where a return on investment is required is very high
- The payout one receives for getting there is increasingly lower
- Diagnostics and, in particular, imaging agents may be an exception
- In the far future, cell-based therapies will provide cures for diseases caused by neurodegeneration and trauma injuries of the brain
- Highly likely they will also lead to brain repair and cure of some mental illness
- These products will generate high investment interest at all stages and will enable a return to the biotech model of the 80's and 90's – meaning the public market will provide both an exit for early investors and a source of capital for emerging blockbusters