

How to Start a Biotech Company

The Trials and Tribulations of Using
Science to Change Healthcare

Resume

Currently Director ePlanet Ventures, CA

- London University, PhD (Pharmacology), '84
- Duke University, MBA '99
- NIMH, NIH Postdoc (neuronal signal transduction) '84-'87
- NIAAA, NIH Visiting Scientist (pharmacogenetics) '87-'91
- Scientist (Department Head), Burroughs Wellcome, Glaxo Wellcome GlaxoSmithKline, '91-'00
- 50 published scientific papers, 4 issued/pending patents
- 3 products to market, 7 drugs in clinical trials (CNS, anesthesia, smoking cessation)
- Co-founded 4 start ups (3 life science companies)

What we'll cover today

- A very brief primer venture capital and biotech
- Decision making processes that we use
- 3 case histories

How did I become a VC?

- My 10 year career at GSK involved analyzing science for product opportunities and steering drugs through the regulatory agencies
- I became involved with ePlanet Ventures, as a scientific advisor in 2000
- The philosophy of the fund is to combine very deep technical and financial expertise with operational experience of running companies

ePlanet Ventures

- Global VC (eight offices: US, China, India, Singapore, UK)
- Our first fund was ~\$640MM ('99)
- Currently raising our second fund
- There are 28 investment professionals + support staff
- Unrestricted Investment Strategy (Mostly IT, ~25% Life Science)
- We seek out companies that have disruptive technology and that can dominate their field
- We participate in all rounds of investments (majority Series B)
- We typically lead the round and usually require a board seat

What is Biotech?

- Using great science to develop products for the treatment of unmet medical needs
- While one goal is to make money for investors, the added benefit is that these products may eventually save lives and/or alleviate morbidity
- In this respect, biotech can provide moral, ethical and financial rewards to all those involved

A Very Brief History of Biotechnology

- 1960- Rational Drug Design (Black, Elion and Hitchings receive Nobel prize)
- 1983 PCR invented at Cetus Co. (Mullis receives Nobel prize; Cetus taken over by Chiron in 1991)
- Genentech demonstrates that DNA cloning can be employed to successfully manufacture human insulin and growth hormone in bacteria in the early 80s
- Amgen makes blood growth factors in the 80s and shows that there are huge markets for biotech products
- Genentech and Amgen's combined market caps approach \$180 billion in 2006, with revenues approaching \$20 billion

Types of Biotech Opportunities

- The main, and most lucrative, type is the therapeutic company: chemicals and biologicals
- Diagnostic companies are a distant second
- “Tool” companies that make research instruments are a third type
- “E-Health” and other information technology companies are the least interesting
- We will focus in this talk on therapeutic companies

How do we make the next Genentech?

Some rules of the game

Stages of Biotech Investing

- Seed Round- extremely early, research project stage-\$100Ks
- Series A- validated science, good IP, partial team, lead compound or exciting new concept-~\$5MMs
- Series B- First time in man (phase I), team in place, small pipeline, phase II plan-~\$20MMs+
- Series C + - completed phase II, phase III plan and/or corporate partner, 2nd drug in phase I- IPO, acquisition, ? \$MMs

Valuation

- This refers to what the company is worth before a funding round (the “pre-money”)
- It has to take into account the founders shares as well as the new employee option pool
- In general, we value series A companies at ~\$4-\$9 MM, depending upon the drug/target, team, previous financings and clinical risk
- Later round valuations vary all over the map and depend on the success of earlier rounds

Major Risks in Biotech Investing (how we make decisions)

- Scientific
- Intellectual property
- Financial
- Clinical
- People
- Competition
- Co-investors

Risks We Won't Tolerate

- Market-there must be a significant unmet need (never hand wave)
- Patient safety, although this depends on the indication. For example, less stringent side effect profiles are allowable for life-threatening indications, such as cancer

How Do We Get Started?

- We see hundreds of business plans per year
- ~95% are triaged immediately due to poor science or insufficient market size
- Triaging based upon science increases the probabilities of financial success dramatically (drugs are a one shot deal)
- Because a company can often take 6 months of diligence to fund, we are very careful about these first, technically-based steps

Scientific Validation

- Modern molecular biology and genetics have highlighted a diversity of great approaches for developing new pharmaceuticals: target validation is critical
- We like the company to come in with a drug-like “lead” or, in rare cases, an exceptional new concept (much higher risk so story must be compelling)
- Even with “sexy” pre-clinical data, we will rarely invest without a clear mechanism of action
- This allows us to quickly eliminate poorly-validated approaches
- Outside experts may be consulted as well

Examples of Companies I Have Started

- Trelion - Founders all from GSK. Formed to out-license an anesthesia product from GSK (phase I)
- Cytospect – Founders (same team as above – 1 + Duke University faculty. Licensed IP for an anticonvulsants from University Washington
- Algebra – Founders ex-Burroughs Wellcome, self generated IP, lead compounds for anti-obesity, validated target
- All of these companies were founded by scientists with ‘deep’ knowledge of relevant science, development process, and target market.

Intellectual Property (IP)

- The second most critical aspect, after the science, as far as a startup
- There are a limited number of targets, so many companies can be chasing the same idea
- IP is the only thing that really protects the small biotech startup from larger biotechs and big pharma
- Thus, IP is analyzed in great depth: a perfectly good scientific investment can die if the IP does not check out
- This is always done by an IP attorney who is a “litigator”, or someone whose job is to demolish patents in court

Financial

- Budgets are extremely important-the company needs to usually ensure that the amount of money they ask for in the “A” round allows them to get through a phase I clinical trial, preferably with hints of efficacy
- Strong co-investors are also important - they need to be financially savvy and have deep pockets for future rounds
- The most important adage is that it will usually take longer and cost more than you think
- This latter point is why we always reserve large amounts of money for follow-on rounds
- Founders should be very careful to neither under- nor overestimate the costs

Clinical

- Because clinical trials are so expensive, a key element is ensuring that a clinical trial can be done in a reasonable period of time for reasonable dollars
- The Phase I trial, which is a safety study, should give an “indication” of efficacy if possible
- This allows for an easier time in raising money for the “B” round, as new investors like to see some hint of efficacy, which validates the company’s approach
- The company needs internal as well as external expertise to ensure that trials are done properly
- Clinical trials are very complex, but they are the heart and soul of a therapeutic company’s success

People

- In one sense, even more difficult and complex than the science
- An excellent and critical technical team is very important
- A leader of that team who is a first rate scientist who has their respect is also important
- A CEO who has some scientific expertise, good money-raising skills, is strategic, charismatic and, most importantly, a friend to the company's scientists
- A supportive board of directors with technical and financial expertise can make an enormous difference to the company's success

Competition

- Any target that has been validated in an important disease area will have competition
- The company needs some technical edge to beat them
- IP is exceedingly important
- A good lead compound(s) or technology are key
- A great team that can execute rapidly and cost-effectively is also critical
- A rapid timeline to clinical efficacy is also desirable

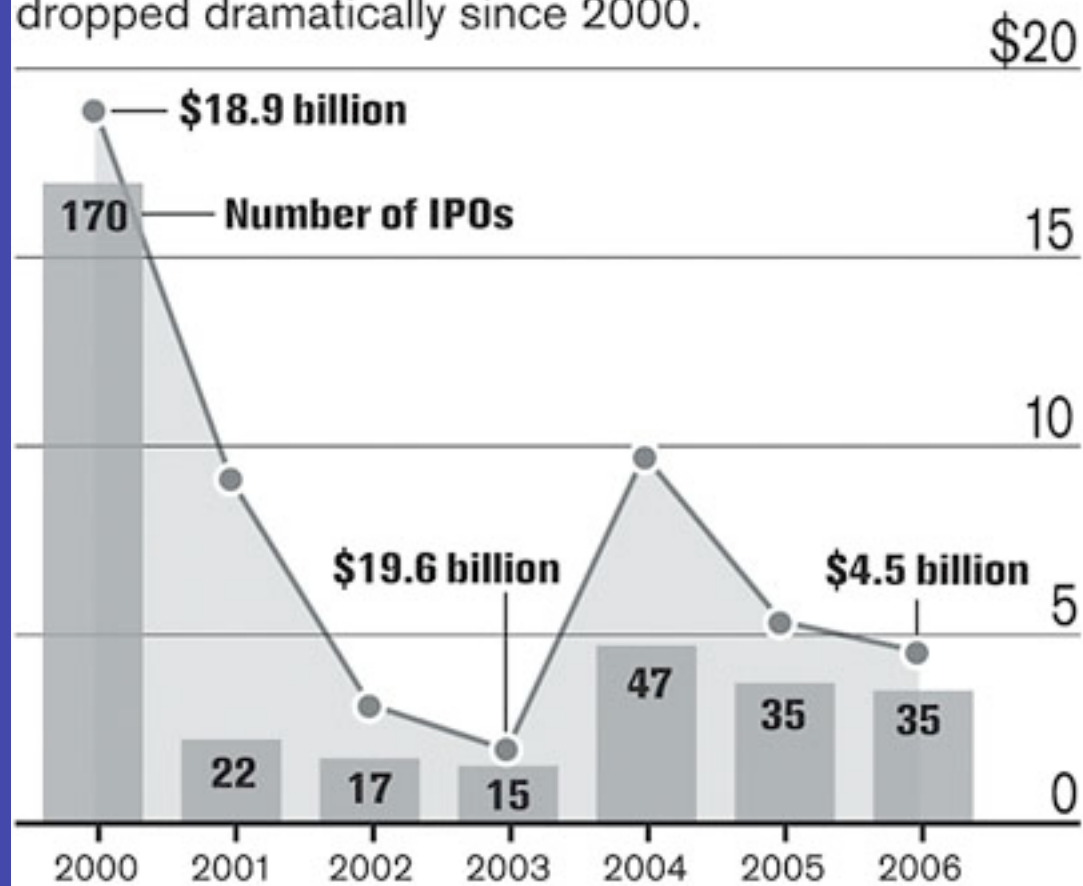
Co-Investors

- Typically a deal is syndicated with a group of venture capitalists
- Everyone in the syndicate needs to be like-minded in most respects (i.e. science, money, strategy, team, etc.)
- Preferably they all need deep-enough pockets to ensure that the company can be funded to an exit
- They need patience and need to be sensitive to the emotions of the people involved in the company

A word about timing

High-tech IPOs

The number and value of high-tech IPOs has dropped dramatically since 2000.



Source: Thomson Financial

The Chronicle

Case History 1: Trelion

- The founders (5) worked together (at GSK) as a team for >5 years prior to founding company – past working relationships are important
- Founders had complementary skill sets and unique knowledge of GSK portfolio
- Founders understood the GSK decision process and were networked into key decision makers - Personal networks are important
- Business plan was to in-license a Phase I drug from GSK
- Strong IP, ‘blue chip’ data and compelling science
- Strong VC interest

Problems

- VC funding and in-licensing agreement had to be executed concurrently
- Company was competing with cash offers for asset
- CEO had no track record
- Team was not ‘battle tested’
- Not a ‘blockbuster indication’

Solutions

- New CEO
- Able to get all parties to agree to simultaneous exchange of agreements
- Company Series A funded ~6/2000 - ~\$9 MM pre-money ~\$16 MM invested, company post money valuation ~\$25 MM

What happened?

- Company still in play, raised > \$50 mm
- Three additional assets in-licensed (different therapeutic areas)
- Lead drug placed on hold by FDA
- Several down rounds
- CEO and team replaced (current CEO is VC partner)

Why did this happen?

- Great scientific, IP and licensing asset
- No internal core competency
- Loss of focus

Case History 2: Cytospect

- Company founders had worked together for > 5 years in previous companies.
- Academic founder had strong IP both for drugs and technology (imaging)
- Good pre-clinical data
- Totally novel target
- Blockbuster, best in class potential

Problems

- Novel target/new theory of disease
- No 'composition of matter' IP
- Low VC interest
- Team too large
- Exclusive license to IP contingent on >\$5 mm VC funding within 12 months

Solutions

- The company raised angel money (\$500K), government grants (SBIR) and State loans.
- Reduced headcount/burn rate (by attrition - two founders left the company to work in academia)
- Renegotiated legal fees and services (into stock warrants)
- Generated NCE's and new 'composition of matter' patents

What happened?

- Company received Series A funding of \$5 MM in two tranches (on a pre-money valuation of ~\$5 MM). Note VC holding = 51% of equity
- VC made selecting a lead compound and obtaining a new CEO conditions for the second tranche
- This should allow the company to complete an investigation new drug (IND) application to the FDA and to be in position to initiate a Phase I clinical trial (subject to series B funding)

Why did this happen?

- Great science
- Strong IP
- Rapid production of leads, successful pre-clinical safety and efficacy testing
- Potential for 'best in class' blockbuster
- Most importantly, a fantastic team of experienced drug developers

Case History 3: Algebra

- A chemistry plan was developed to address critical shortcomings of failed obesity drugs
- The founders are inventors of the previous drugs and took part in most FDA discussions
- The company developed strong broad and specific IP
- The company generated compelling pre-clinical data
- Plan A is to seek early corporate partner

Major Risks

- The previous drugs in the class failed!
- Under funding
- Significant competition

Solutions

- Fully understand why previous drugs failed and present compelling solutions based on science
- Virtual model
- Very narrow business plan (focus, focus, focus)
- Identify corporate champions and leverage personal contacts/knowledge of big pharma decision making

What Happened?

- The company is in advanced discussions with several big pharma companies - I'll keep you posted!

Summary

- Biotech startup investing is very complex, but careful scientific analysis dramatically increases the probabilities of success
- Good IP is essential
- An experienced team is a must
- Clinically relevant data in the A round and/or proof of a major new concept(s) are key
- A realistic budget and timelines are critical
- Sophisticated and patient co-investors are important

Acknowledgements

- Larry Lasky
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TYPICAL FINANCING PROGRESSION FOR A MEDICAL DEVICE COMPANY

<u>Round</u>	<u>Amount</u>	<u>Who Provides</u>	<u>What is needed</u>	<u>Use of Funds</u>
Seed	< \$1 (millions)	Individuals; Angels; Incubator; a VC firm; Friends & family	Idea, with a little research; Proof that laws of medicine, physics, hemodynamics, mechanics, are not violated; Maybe an enthusiastic doctor	bench work; prototypes; IP filings; maybe some animal testing
Series A	\$4 - 5	Expect two VC firms (or other institutional investors) splitting the round 50/50	Some crude prototypes and testing; Simple analysis showing a big market; Initial IP position	Design, build, test looping; Animal testing; Refined prototypes that could be used in man; Maybe early human studies.
Series B	\$10 - 12	One additional VC takes ½; existing two VCs split the other half	Clinical proof of feasibility (or doesn't fail), preferably in humans; Start on management team; Reasonable IP position and strategy; Clinical advisors; Development plan, budget, timeline, etc.	A working product that gets used in serious clinical testing in man. European regulatory filing or approval.
Series C	\$20 - 30	Mezzanine VC firms, corporate investors	Significant human experience; Clear path to sales; Physician enthusiasm; US approval or filing for clinical trials	Clinical trials for FDA regulatory approval; FDA filing or approval.
Series D	??	same	Significant human data; European sales; FDA trials completed; US approval??	For more expensive projects, a full product launch. Takes company to at least break-even.
IPO	\$50 (or more)	Public	Increasing sales; several qtrs. of profits	Marketing; sales force expansion; R&D
Acquisition	?	larger corporation	For existing markets, sometimes just good clinical results. For new markets, prove the market exists via sales growth.	