What to Expect in Biotech
(and Pharma)

Douglas Kalish, Ph.D.
What you learn as an academic

- Knowledge is an end in itself
- Don’t reveal all that you know
  - In grant applications or publications
- Today’s collaborator can be tomorrow’s competitor
- The less you depend on other people the faster your research will go
But to succeed in business, you need to be...

- Driven by profits
- Aware of the needs/characteristics of the market
- Focused on products, not interesting science
- Collaborative internally
- Competitive externally
Making the Transition from College to the Real World

Workshops, eBooks, and links to help you survive and thrive in your first job.

Congratulations on leaving or getting ready to leave college, grad school, or your post-doc. You've learned a lot, had fun and made friends. Now you're looking for a job and the reality is sinking in... College hasn't fully prepared you for the Real World. Relax, and welcome to dougsguides: a set of eBooks, workshops, and links to help you find a great job with great
The training that BioScientists need (consensus)

• Overview of drug development process
• Business basics (profit requirements)
• Team skills
• Conflict resolution
• And later, management skills, negotiation, project management, budgeting
The lack of business vision leads to

“Scientists wanting to pursue science for knowledge sake... Not advancing our commercial objectives... Falling in love with research program... Unaware of experimental critical path... Results don’t affect our commercial path... Wasted time from non-communication... No team orientation; not communicating things that rest of team should know... Not calling for help... People in leadership positions without skills or training.”
Business Survival Skills

- Understanding the difference between pure science and drug development
- Appreciating how market forces affect development strategies
- Understanding the difference between investors (or shareholders) and NIH and NSF
The Drug Development Process

Entry into the drug development process
Look for differences (protein, DNA, mRNA, enzyme activity) between normal and diseased tissue
Business Strategies Affect Target Selection

- Concentrate on disease (cancer, obesity, cardiac)
- Concentrate on tissue (lung, breast, brain)
- Concentrate on therapies (RNAi, kinases)

- Do we have a proprietary technology?
- How big is the market?
- What is the competition?
- What experience do we have?
- Is there synergy with our other products?
Verify the involvement of the protein in the disease state. Understand the protein pathways and interactions.
Evaluate leads to ‘cure’ the problem, e.g.:
• Replace missing or defective protein with gene therapy
• Anti-sense RNA to prevent protein expression
• Antibody to remove protein
• Stimulation of synthesis to replace protein
Re-visit the Business Issues

- Does the putative therapy fit with our business strategy?
- Exactly what disease(s) will the therapy be directed to?
- What stage(s) of the disease will the therapy target?
- How will the drug be delivered?
- Do we have in-house experience with the technology?
- Will the therapy be better than existing treatments?
- Do we have the expertise to manufacture the drug?
- Do we have the expertise to market the drug?
- What are the expected profits? How much can we charge?
- What are the risks and how can they be mitigated?
The Drug Development Process

- Drug Candidates
- Target ID
- Target Validation
- Lead Discovery
- Pre-Clinical
- Clinical Phase I
- Clinical Phase II
- Clinical Phase III
- Manufac-turing
- Distribution

Animal tests of toxicity and efficacy of therapy
Small group of healthy volunteers (10’s) to determine safety and toxicity. Maybe some members of target group
The Drug Development Process

100’s of patient population to determine dosage, safety
The Drug Development Process

1000’s of patients to determine efficacy, dosage, safety, side effects, and interactions
The Drug Development Process

- Drug Candidates
- Target ID
- Target Validation
- Lead Discovery
- Pre-Clinical
- Clinical Phase I
- Clinical Phase II
- Clinical Phase III
- Manufacturing
- Distribution

Scale up to manufacture commercial quantities
The Drug Development Process

- Drug Candidates
- Target ID
- Target Validation
- Lead Discovery
- Pre-Clinical
- Clinical Phase I
- Clinical Phase II
- Clinical Phase III
- Manufacturing
- Distribution

Detailing, advertising and distribution. Insurance company reimbursement
The Dreaded Phase IV: Reporting adverse consequences
Compound Success Rates and Timing by Stage

- **Discovery** (2-10 Years)
- **Preclinical Testing**
  - Phase 1: 10’ s of volunteers
  - Phase 2: 100’ s of patients
  - Phase 3: 1000’ s of patients
- **FDA Approval**

Success Rates:
- 5,000 – 10,000 Screened
- 250 enter Preclinical testing
- 5 enter clinical testing
- 1 approved

Source: Phrma.org

Copyright 2012, Doug Kalish. All rights reserved.
Why don’t all targets generate therapies?

• Just doesn’t work (of mice and men)
• Similar symptoms from different causes
• The cure is worse than the disease
• ADME/tox: absorption, distribution, metabolism, excretion/toxicity
• Most diseases have complex causes
• Diseases have a time course
• Individual differences in drug metabolism (pharmacogenomics)
• …and so on
How much does it cost to get a drug approved?

![Graph showing annual profit (loss) over years.](image-url)
How much does it cost to get a drug approved?

Cumulative Profit/Loss per Year

Profit (Loss) in Millions

Year
Summary of Drug Development Risks

- Scientific – Does it work?
- Commercial – How big is the market?
- Competitive - Does someone else have a better product, now or in the future?
- Time to market – How long does your patent have to run?
- Intellectual Property position – Do you have all requisite licenses? Have you excluded all others from using the IP?
Mitigating the Financial Risks in Drug Development

• Killing unpromising candidates at the earliest opportunity
• Maintaining marketing exclusivity as long as possible
• Populating a product pipeline
• Spreading the risk
Fully Integrated BioPharma Company (FIBCO)

- Robust pipeline of products needed at all stages
- 100-1000x number of expected products entering the pipeline each year
- Resources: cash, facilities, expertise at all stages of drug development process
- Strong FDA relationships
- Strong marketing and distribution functions
- Strong IP function to protect and extend exclusivity of products
- Ability to forecast drug marketplace 5-10 years out
Realities of the Pharma/Biotech Industry

• It is extremely difficult to build a new fully integrated biopharma company
• Successful companies need portfolio of products in different stages of development
• Risks of drug development need to be strategically managed (partnerships, joint ventures, out-licensing)
• Successful companies – big and small - need partners in all phases of the drug development lifecycle
• Companies are specializing in all phases of the value chain
Dis-Integration of Drug Discovery

Drug Candidates  Target ID  Target Validation  Lead Discovery  Pre-Clinical  Clinical Phase I  Clinical Phase II  Clinical Phase III  Manufac-turing  Distribution

Drug Discovery  Animal Studies  Clinical Tests  Commercialization
Life at a FIBCO

• “Big company” experience, resources, benefits
• Lots of people to learn from
• Well-established policies and bureaucracy
• You will probably be well-removed from the important decision-making
• Mergers, acquisitions, layoffs and retrenching are becoming more common (300,000 jobs lost since 2000; but 40% increase predicted to 2018)
Characteristics of Biotech Companies

- Primary assets are intellectual not physical
- Capital intensive, not labor intensive
- Highly skilled labor needed
- Long-term paybacks
- Legal uncertainty
- Hard to value
- High burn rates
- Global competition

Equals: High Risk, High Return
Life at a startup

• There is never enough money
• There are never enough people
• There is never enough time
• Doing one job may not be enough
• Uncertainty rules
• Perks can be cool
• Reality sucks
Research and Non-Research Positions for PhDs/Postdocs

- Patent agent, advisor, USPTO
- Research Analysts/Assoc
- Consultant
- Bioinformatics
- Quality Control
- Startups
- M&A, Portfolio Mgt
- Market Comms
- Tech Support, Trainer
- Scientist I
- Project coordinator
- Medical writer, IT
- FDA, Liaison
- Scientific affairs
- Market research
- Technical sales rep
Hot tech skills in drug development - today

Genomics → Functional Genomics → Target ID → Target Validation → High Throughput Screening

- Genomics
- Functional Genomics
- Target ID
- Target Validation
- High Throughput Screening

Clinical Trials → Development Candidates → Lead Optimization → Chemistry

- Clinical Trials
- Development Candidates
- Lead Optimization
- Chemistry

- Bioinformatics
- Expression arrays
- Positional cloning
- Proteomics
- Transgenes
- Knockouts
- siRNA
- Animal models
- Disease models
- Nanotechnology
- Robotics
- Disease models
- Nanotechnology
- Microassays
- Detection systems
- Statistics
- Big Data
- Trial design
- ADME
- Toxicology
- Scale-up chemistry
- Structure based design
- Computational biology
- Cheminformatics
- Combinatorics
- Cheminformatics
- Chemical libraries

Source: Lehman Bros
Don’t forget:
Non-tech skills are required, too

• Communication and presentation
• Interpersonal skills
• Basic understanding of drug development and business
• Desire to pursue the product, not the science
Making yourself desireable

- Find a human disease aspect to your research
- Concentrate on areas of interest to industry
- Acquire technical skills of interest
- Concentrate on the 4 P’s: publications, presentations, posters and patents
- Understand the drug development process
- Understand industry issues: e.g. generics, biosimilarity, assay development (visit pharma.org, bio.org)
- Attend trade conferences
• Specific industry knowledge

• ‘How-to-get-a-job’ websites
  – sciencecareers.sciencemag.org
  – www.dougsgguides.com/nowwhat

• General business knowledge
  – www.dougsgguides.com/businessbasics

• Presentations and communications
  – www.toastmasters.org
The Bottom Line

Without a business context, you may do good science…

…but you can’t do good drug development
Stay in touch:

- Register and comment at dougsguides.com
- ‘Like’ dougsguides on FB
- Follow @dougsguides on Twitter
- Connect with Doug Kalish on LinkedIn