Transitioning from Big Pharma to a Start-Up: Opportunities and Challenges

Mark Dresser, PhD
Denali Therapeutics
Presentation Overview

• Roles for Clinical Pharmacologist within a start-up/early-stage biotech

• Experience that Clinical Pharmacologists can bring from a large company

• Opportunities and challenges at a start-up/early-stage biotech

• Critical points to evaluate at a (start-up/early-stage biotech) company

• Making the jump .... When? Why? How? Who/What?
Roles for Clinical Pharmacologist within a start-up/early-stage biotech

• Depends on one’s experience, expertise, willingness to grow, .....  

• At large companies, Clinical Pharmacologist can gain experience in  
  • Early and Late Clinical Development and Regulatory  
  • Different Therapeutic Areas and modalities (eg, biologics, small molecules, ...)  
  • Project leadership and management  

• At start-up/early-stage companies, roles could expand to include  
  • Clinical Pharmacology (study designs, PKPD, DDIs, formulation strategies, ...)  
  • Biomarkers, Bioanalytical, CMC, DMPK, Preclinical Safety, Regulatory, ....  
  • Leading project teams and/or management  
  • Contribute to building a new company
Experience that Clinical Pharmacologists can bring from a large company

- “Real-world” drug development know how
- Complex problem solving
- Sound decision making
- Effective collaborations
- Prior experience in building new technical areas/teams is helpful
Opportunities and challenges at a start-up/early-stage biotech

• **Opportunities**
  • **Contribute** in a much broader way to a drug development effort
  • **Participate** in building a new company
  • **Expand** your expertise beyond Clinical Pharmacology
  • **Apply** what you have learned from your previous experiences

• **Challenges**
  • **Focus** – critical that the company has a clear a focus and vision and priorities
  • **Organization** – need to put in place foundational organization and get it right the first time
  • **Managing growth** – people and projects
Points to Evaluate:
Rationale for starting a new company

THE TIME IS RIGHT

SCIENTIFIC DRIVERS:
• Science breaking open
  - Human genetics informing Degenogenes
• Crossing the BBB within reach
• Biomarkers informing drug development

BUSINESS PRINCIPLES:
• Learning from oncology
• The right team and approach
Points to Evaluate:
Company’s Scientific Strategy

DENALI’S THREE SCIENTIFIC PRINCIPLES

- Mining Genetic Pathway Potential
- Engineering Brain Delivery
- Biomarker-Driven Development

RIGOROUS APPROACH FOR INCREASED PROBABILITY OF SUCCESS
Points to Evaluate: Company’s Business Strategy
(18 months; 5 years; 10 years)

**DENALI BUSINESS PRINCIPLES**

**Portfolio Approach**
- Broad portfolio of programs
- Core and Seed prioritization
- Novel targets in validation

**Parallel Investments**
- Back-up molecules for all programs
- Pick best molecules for Ph2/3

**Strategic Partnering**
- Strong network of partners in industry and academia
- Share cost and risk

Example: LRRK2 program

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Phase</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNL201</td>
<td>Lead</td>
<td>Ph1b(PD)</td>
</tr>
<tr>
<td>DNL151</td>
<td>Backup</td>
<td>Ph1 HV</td>
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</tbody>
</table>

**DENALI MECHANISM**

- [Takeda logo]
- [Sanofi logo]
Points to Evaluate:
Board of Directors, Leadership, Team

THE DENALI TEAM

SCIENTISTS AND DRUG DEVELOPERS

190+ BASED IN SOUTH SAN FRANCISCO

BOARD OF DIRECTORS

VICKI SATO (CHAIR)
DOUG COLE
PETER KLEIN
DAVID SCHENKMAN
RYAN WATTS

MARC TESSIER-LAVIGNE
JAY FLATLEY
ROBERT NEILSEN
JENNIFER COOK
GRAIL

SENIOR LEADERSHIP

RYAN J. WATTS, PHD – CEO
• Previously built and led Genentech’s neuroscience strategy, portfolio and research department
• Stanford University, PhD Biological Sciences

ALEXANDER SCHUTH, MD – COO
• Formerly head of Genentech’s BD groups for neuroscience and discovery technologies
• Previously Merrill Lynch ECM (London)
• Charite Medical School (Berlin) MD, Wharton MBA

CAROLE HO, MD – CMO
• Formerly VP Early Clinical Development at Genentech
• Previously Medical Director at J&J and clinical neurologist at Stanford
• Cornell Medical School, MD; Neurology Residency, Harvard

STEVE KROGNES – CFO
• Formerly CFO Genentech and Head of M&A Roche
• Previously Goldman Sachs and McKinsey
• Harvard Business School MBA, Wharton

DANA ANDERSEN, PHD – CTMO
• Formerly VP and Global Head of Technical Development Project & Portfolio Management, Genentech/Roche
• Stanford University, PhD Chemical Engineering
Points to Evaluate: Finances and Finance Strategy

**Building a High Quality Shareholder Base**

<table>
<thead>
<tr>
<th>SERIES A</th>
<th>SERIES B</th>
<th>INITIAL PUBLIC OFFERING</th>
</tr>
</thead>
<tbody>
<tr>
<td>MID-2015</td>
<td>MID-2016 / Q3 2017</td>
<td>END-2017</td>
</tr>
<tr>
<td>$219 MILLION</td>
<td>$160 MILLION</td>
<td>$288 MILLION</td>
</tr>
</tbody>
</table>

**Partners**

- ARCH VENTURE PARTNERS
- ALASKA PERMANENTE FUND
- FLAGSHIP PIONEERING
- F-PRIME
- Crestline
- FBRI
- BAILLIE GIFFORD
- TEMASEK
- Fidelity
- Baron Capital
- GIC
- INVUS
Making the jump .... Why? Who/What? When? How?

• At some point in the future, you may want to consider a move from a large organization to a start-up of a small company

• Recommend thinking carefully about .....  
  • Why?
  • Who/What?
  • When?
  • How?
Acknowledgements

• My colleagues and mentors at
  • Denali Therapeutics
    • Start-up in 2015 => early-stage company in 2018
  • Genentech
    • Large biotech
  • ALZA => Johnson & Johnson
    • Mid-size company acquired by a big pharma