

A large, colorful molecular structure composed of various spheres (blue, green, red, orange, yellow, pink, white) connected by thin white rods, set against a light blue background. A faint, light blue silhouette of a human head is visible behind the structure. The text "FROM MOLECULE TO PATIENT" is overlaid on the right side of the image.

FROM
MOLECULE TO
PATIENT

ASCPT 2019
ANNUAL MEETING



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

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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

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MOLECULE TO
PATIENT

- “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**



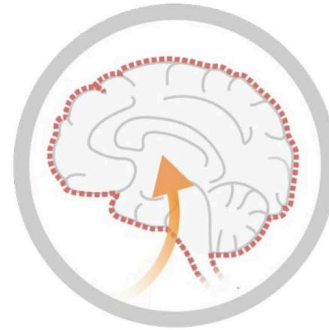
Points to Evaluate: Company's Scientific Strategy

DENALI'S THREE SCIENTIFIC PRINCIPLES

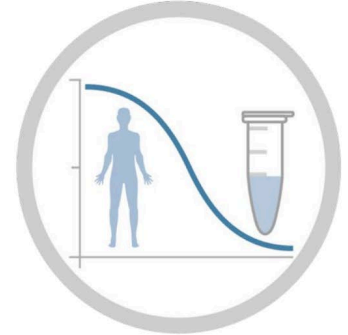
Mining Genetic
Pathway Potential



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

PROGRAM/TARGET	MOLECULE	INDICATOR	PROGRESS TRACKER				PARTNER
			Discovery	Preclinical	Phase 1	Phase 2	
LESION/PROTEIN TARGETS							
LEP1	DNL151	Pathogenesis	██████████	██████████	██████████		
LEP2	DNL151	Pathogenesis	██████████	██████████	██████████		
LEP3	DNL151	Pathogenesis	██████████	██████████	██████████		
LEP4	DNL151	Pathogenesis	██████████	██████████	██████████		
LEP5	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
CELLULAR/METABOLIC TARGETS							
LEP6	DNL151	Pathogenesis	██████████	██████████	██████████	Sanofi	
LEP7	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP8	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP9	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP10	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP11	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP12	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP13	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP14	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP15	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP16	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP17	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP18	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP19	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	
LEP20	DNL151	Pathogenesis	██████████	██████████	██████████	Takeda	

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

Parallel Investments

Example: LRRK2 program

Molecule	Phase	Status
DNL201	Lead	Ph1b (PD)
DNL151	Backup 1	Ph1 HV

- 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

Points to Evaluate: Board of Directors, Leadership, Team

THE DENALI TEAM

SCIENTISTS AND DRUG DEVELOPERS



190+ BASED IN SOUTH SAN FRANCISCO

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



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JAY FLATLEY
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ARCH Venture Partners



JENNIFER COOK
GRAIL

Points to Evaluate: Finances and Finance Strategy

BUILDING A HIGH QUALITY SHAREHOLDER BASE

SERIES A		SERIES B		INITIAL PUBLIC OFFERING	
MID-2015	\$ 219 MILLION	MID-2016 / Q3 2017	\$ 160 MILLION	END-2017	\$ 288 MILLION



ARCH VENTURE PARTNERS

ALASKA PERMANENT FUND

FLAGSHIP PIONEERING
SCIENTIFIC VENTURES FOR LIFE

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Crestline

FBRI
A division of F-Prime



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ALASKA PERMANENT FUND

QIA
QATAR INVESTMENT AUTHORITY



Nasdaq

Fidelity INVESTMENTS

BAILLIE GIFFORD

ALASKA PERMANENT FUND

TEMASEK

GIC

BARON CAPITAL

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