Accelerating Treatments to Patients: The Experience of an Academic Spin-Out

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Disclosures

- $C_2N$ Diagnostics
About C₂N Diagnostics

- Formed in late 2007 by Professors Randall Bateman and David Holtzman (Wash U School of Medicine [WUSM], St. Louis, MO), and LifeTech Research
- Management and scientific team; C₂N occupies ~4,500 sq. ft. of lab / office space in St. Louis, MO
- Owner or exclusive licensee to > 30 issued or pending patent applications and registered trademarks worldwide relating to the core technology platforms
- Private-public partnerships to advance goals

Mission

Commercialize unique technologies to better detect, monitor, and treat Alzheimer’s disease and other neurodegenerative disorders
**Business Strategy**

**Business Segments**
1. Diagnostics – Preclinical detection / Therapeutic monitoring
2. Disease-modifying therapeutics for neurodegeneration

**Business Plan**
1. Large-scale clinical validation studies of SILK™/SISAQ™ Assays
2. GLP → CLIA → IVD and novel biomarkers
3. First in man (FIM) study for lead therapeutic

Establishing innovative partnerships with;
- Pharmaceutical companies
- Diagnostic and analytical tools companies
- Vendors within the supply chain
- Disease research foundations
- Academic centers

to accelerate commercialization of technologies.
SILK™: The Nidus for C₂N’s Formation

• *In vivo* measurements of the kinetics/metabolism of brain-derived proteins and other biomolecules

• New window into CNS disorders of protein accumulation and impaired clearance (e.g., AD, PD, HD, FTD).

• Measure rates of biomolecule metabolism to determine normal physiology, pathophysiology, and treatment effects.

• Understand the physiology of CNS protein kinetics and changes that may lead to failure of normal mechanisms.
SILK-Aβ® Measures Kinetics of Newly Generated Aβ (Fractional Turnover)

(Source: Bateman et al., Nature Medicine 2006; 12:851-6; Bateman et al., JASMS 2007; C2N Diagnostics)
Independent Validation of *In Vivo* Kinetics of $^{13}\text{C}_6$-Labeled Aβ

Total Aβ Kinetics in 5 Healthy Volunteers

Source: C$_2$N Diagnostics, LLC
Defining the “Diagnostic” Product: Development, Validation, and Logistics

Components of a SILK-Aβ® SPOT Test Kit

Subject arrives at MD office (or clinical lab site) following overnight fast

"SILK-SPOT Aβ® Test Kit" opened and 13C6-Leu bolus dosed to subject

Blood sample collected and plasma prepared

Plasma sample shipped to analytical lab (e.g., C2N)

Plasma sample is logged in and analyzed

Reference Lab reports results back to MD
Expansion of Product Portfolio at C2N → Consistent with Company’s Mission

- Library of murine antibodies directed against tau protein \(^1,^2\), developed in the laboratory of Dr. David Holtzman at WUSM → exclusively licensed to C2N

- C2N advanced tau antibodies through further characterization, testing, and development


- Generous funding support of Phase 1 study from Part The Cloud (Alzheimer’s Association) testing ABBV-8E12 (formerly C2N-8E12) in patients with PSP

- Now in two Phase 2 clinical studies: one in AD and one in PSP

1) Yanamandra et al., Neuron 2013; 80(2):402-410
2) Yanamandra et al., Ann Clin Transl Neurol 2015; 2(3): 278-288
Randomized, double blind, placebo controlled, single ascending dose (SAD) study

Study Objectives: Evaluation of the safety, tolerability, immunogenicity, and PK of single-dose of C$_2$N-8E12 (dose range from 2.5 – 50 mg/kg)

Sample size of 30 subjects with PSP: 24 drug, 8 placebo

- Acceptable safety profile with no clinically concerning trends in number of severity of AEs between placebo and dosed patients
- Plasma half-life and CSF:plasma ratio consistent with other humanized mAbs
A Few Lessons Learned

Source: Adapted from Paul Graham’s (Y-Combinator) StartUp Curve, www.ventureburn.com
Key Ingredients
Team Construction

- Models are wide-ranging (Completely virtual to fully integrated teams)

- Strong compatibility necessary between founding scientists and business partners

- Technology transfer can be optimized with (i) hiring individuals who bring continuity to the project; and (ii) independent replication of data as soon as possible

- Great project managers are necessary to manage outsourced processes

- A good lawyer engaged early can save future trouble and costs

- Experienced operators derive satisfaction from providing mentorship and advisory support
Sourcing the Capital

Key Questions

- What unmet medical need does your technology address?
- Who has unique interest?
- What is your timeline?
- What are your capital requirements?
- Are you building a product or a company?
- What are your own goals?
- Beyond capital, what do you need?
- What is driving your prospective investor(s) interests?
Lessons Learned on Raising Capital

- Surround yourself with as many smart people as possible
- Know what you want before you ask investors
- Define your value milestones and assume accountability
- Be passionate and dispassionate at the same time
- Behind every investment champion, there is a critic
- Perception is reality to investors, so understand the perception
- Seek profitability as soon as possible → this creates options
- Raising capital is not easy and it never really ends
- Evidence drives not only clinical adoption, but also investment and business development success
Expert Risk Management Drives Commercial Success

Technology Risk
- Single product vs. a technology platform?
- Stage of development – early feasibility or reproducible & robust?

Market Risk
- “Red ocean” or “blue ocean” opportunity?
- Where is the unmet need?
- Who will pay?

Intellectual Property
- Crowded or clear?
- Patentability? Freedom to Operate?
- A single provisional or a picket fence?

Regulatory Risk
- NDA
- PMA vs 510(k)
- CE Mark

Financing Risk
- Macroeconomy and microeconomy
- Cash runway & time / cost to achieve key milestones
- Exit strategy defined early with flexibility to adapt

Management Risk
- Experience and decisiveness
- Risk tolerance?
- Compatability
Team Members
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