Rare Disease Partnerships

A Model for a New Era of Drug Development

IRDiRC
April 2013

Cristina Csimma, PharmD, MHP
Rare Disease Partnerships
a model for a new area of drug development

• Rare diseases in the current drug development and funding context

• Examples of novel partnerships and models to facilitate translation
Call for a radical change in R&D thinking

"Our industry is taking too long, we're spending too much, and we're producing far too little...Ironically, the crisis in our innovation model comes at a time when we have vastly more scientific knowledge and data than ever before....need to be more entrepreneurial and globally networked. That means turning to partners for molecules, funding... with greater efficiencies.”

John Lechleiter, CEO Lilly, FierceBiotech 10 Feb 2011

“The research and development landscape has changed, and a new model is needed. ...the serious challenges that currently confront the private sector may make it difficult to capitalize on new opportunities....partnership with the private sector are essential for this translation to succeed.”

Francis Collins, Director NIH, Science Translational Medicine July 2011
R&D in orphan diseases

- New biologic insights:
  - Greater understanding of disease pathology, genomic tools, even sub-setting of large diseases
  - Pathways driving treatments; ability to match drug to biology
- Rare disease R&D funding is up despite large overall reductions
- Rare and orphan diseases offer a compelling model for drug development and commercialization
- Smaller, focused programs allow small biotech’s to take to commercial stage, more opportunities to pursue programs
- To make informed, earlier development decisions:
  - Increased scrutiny of preclinical data
  - Increased scrutiny of clinical trial design and size
# Pharma & Biotech Interest in Rare Disease

<table>
<thead>
<tr>
<th>Date</th>
<th>Acquirer / Licensor</th>
<th>Target / Licensee</th>
<th>Indication</th>
<th>Epidemiology</th>
<th>Stage</th>
<th>Upfront</th>
<th>Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb 13</td>
<td>Roche</td>
<td>Chiasma</td>
<td>Acromegaly, NET</td>
<td>40K US + EU5</td>
<td>P3</td>
<td>$65M</td>
<td>$530M</td>
</tr>
<tr>
<td>Jan 13</td>
<td>Shire</td>
<td>Lotus</td>
<td>Dystrophic Epidermolysis Bullosa</td>
<td>~2K WW</td>
<td>PC</td>
<td>$49.5M</td>
<td>$275M</td>
</tr>
<tr>
<td>Jan 13</td>
<td>Pfizer</td>
<td>Repligen</td>
<td>Spinal Muscular Atrophy</td>
<td>Incidence 1/15K live births</td>
<td>P1</td>
<td>$5M</td>
<td>$65M</td>
</tr>
<tr>
<td>Feb 12</td>
<td>Shire</td>
<td>FerroKin</td>
<td>Myelodysplastic Syndrome</td>
<td>Incidence 10-20K/year</td>
<td>P2</td>
<td>$100M</td>
<td>$225M</td>
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<tr>
<td>Feb 12</td>
<td>GSK</td>
<td>Angiochem</td>
<td>Enzyme delivery to the brain</td>
<td>Various LSD/MPS II</td>
<td>PC</td>
<td>$5M</td>
<td>$270M + royalties</td>
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<tr>
<td>Dec 11</td>
<td>Alexion</td>
<td>Enobia</td>
<td>Hypophosphatasia</td>
<td>1/100K live births; 2-4K WW</td>
<td>P3</td>
<td>$610M</td>
<td>$410M</td>
</tr>
<tr>
<td>Oct 11</td>
<td>Pfizer</td>
<td>Glycomimetics</td>
<td>VOC associated with SCD</td>
<td>30-40K US; 75K hosp. vis.</td>
<td>P2</td>
<td>N/A</td>
<td>$340M</td>
</tr>
<tr>
<td>Jan 11</td>
<td>Alexion</td>
<td>Taligen</td>
<td>Paroxysmal Nocturnal Hemoglobinuria</td>
<td>8-10K US + Western EU</td>
<td>PC</td>
<td>$111M</td>
<td>N/D</td>
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<tr>
<td>Sep 10</td>
<td>Shire</td>
<td>Acceleron</td>
<td>Duchenne Muscular Dystrophy</td>
<td>8K US</td>
<td>P2a</td>
<td>$45M</td>
<td>$450M</td>
</tr>
<tr>
<td>Sep 10</td>
<td>Pfizer</td>
<td>FoldRx</td>
<td>TTR Amyloidosis</td>
<td>8K WW</td>
<td>P3</td>
<td>$210M</td>
<td>$455M</td>
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</tbody>
</table>
Regulatory Environment

• 200 orphan drugs enter development today, vs. one per year in 1983

• Approximately one third of approvals are for orphan products

• FDA Safety and Innovation Act (FDASIA) allows more rapid and flexible pathways for drugs targeted at orphan patient populations
  – “FDA is more accessible. The relationship reduces the burden of uncertainty…”
    Joseph Markmann, PWC
  – Reauthorizes two programs that encourage pediatric drug development

• New initiatives include accelerated approval and breakthrough designation for certain innovative drugs
  – “‘Breakthrough therapies’ initiative could cut the process of drug approval to one stage with 30-50 patients.” – Dr. Janet Woodcock (CDER)
  – “Create trial networks of expert doctors and community physicians...In these networks, therapies coming out of dose-finding Phase I studies can quickly be tested for efficacy in patients.” – Dr. Janet Woodcock (CDER)
  – Huge opportunity for an orphan drug company; beyond the designation, encourages (unprecedented) access to senior level FDA clinicians for development input
Rare Disease Partnerships
a model for a new area of drug development

- Rare diseases in the current drug development and funding context

- Examples of novel partnerships and models to facilitate translation
New models of collaboration are emerging

• Public-private partnerships
• Foundation funding playing increasingly impactful role
• Non-profits collaborations
• Venture capital-CROs
• Targeted investments such as disease, geography
• Shared/centralized databases
  – More powerful data mining
• Standardized clinical care as basis for clinical research
• International involvement
• Regulators playing a role
## Innovative Collaborations…

<table>
<thead>
<tr>
<th>Innovator</th>
<th>Collaborator(s)</th>
<th>Announced</th>
<th>Focus</th>
<th>Stage</th>
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<tbody>
<tr>
<td>GSK</td>
<td>Imagine Institute</td>
<td>Nov 2012</td>
<td>Netherton Syndrome</td>
<td>Early stage</td>
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<tr>
<td></td>
<td>Necker Hospital</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Shire</td>
<td>Boston Children’s</td>
<td>Nov 2012</td>
<td>Rare pediatric diseases</td>
<td>Develop candidate &lt;3 years</td>
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<tr>
<td>Pfizer</td>
<td>CF Foundation Therapeutics,</td>
<td>Nov 2012</td>
<td>Cystic Fibrosis (ΔF508 mutation)</td>
<td>Early to late stage</td>
</tr>
<tr>
<td></td>
<td>Inc.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TVM Capital</td>
<td>Chorus (Lilly unit)</td>
<td>Oct 2012</td>
<td>All therapeutic areas</td>
<td>Candidate selection → POC</td>
</tr>
<tr>
<td>Shire</td>
<td>Fondazione Telethon</td>
<td>Oct 2012</td>
<td>Rare diseases</td>
<td>Early stage research &amp; Tx</td>
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<tr>
<td>TVM LSV VII</td>
<td>Quebec</td>
<td>May 2012</td>
<td>Single asset co.</td>
<td>Early stage</td>
</tr>
<tr>
<td>Flagship Ventures</td>
<td>Merck</td>
<td>April 2012</td>
<td>Areas of unmet medical need</td>
<td>Early stage Co</td>
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<tr>
<td>Index Venture</td>
<td>GSK, J&amp;J</td>
<td>Mar 2012</td>
<td>European focus; asset centric</td>
<td>Early stage Co</td>
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<tr>
<td>Atlas Venture</td>
<td>Shire</td>
<td>Dec 2011</td>
<td>Rare genetic diseases</td>
<td>Early stage Tx</td>
</tr>
</tbody>
</table>
A Novel International, Multidisciplinary Partnership to Enable Drug Development in Rare Diseases

TACT and PPMD

C Csimma, PharmD and S Hesterlee, PhD
TREAT-NMD and PPMD Partnership on TACT

Who we are:

• **TREAT-NMD**: global network of excellence - EU-funded roots
  – Advancing diagnosis, care and treatment for neuromuscular disease (NMD)
  – Advisory committee for Therapeutics (TACT) established to evaluate potential therapies in an objective, comprehensive manner

• **PPMD** (Parent Project Muscular Dystrophy): US largest non profit organization focused on Duchenne Muscular Dystrophy (DMD)
What is TREAT-NMD

- A “network of excellence” initially funded by the European Union (but with global collaborations)
- Aims to help promising new treatments for neuromuscular diseases make the transition from the lab to the patient
- Not a research project but an infrastructure project
- Creating the “tools” for trial-readiness in the neuromuscular field
- Helping researchers and expert centres collaborate better
- Improving patient care worldwide

➢ *Sustained beyond 2011 as TREAT-NMD Alliance*
TREAT-NMD TACT Initiative

- TACT established in 2009
  - Volunteer experts from academia, industry, non-profit, patient advocacy to provide development advice, NIH and FDA members
- Provides development advice to academia and industry
- Eliminates historical barriers between academia, industry, patient organizations
- Multidisciplinary, comprehensive input
- Reviews are confidential
- Addresses translational gap in NMD
- Independent of funding stream
- PPMD partnered with TACT and integrated TACT reviews in its diligence for funding
- TACT is directly addressing the IRDiRC principles and goals
What TACT is addressing

- Fragmented and subjective approach to funding translation in NMD
- Lack of comprehensive review of both science and development potential of compounds
- Rigor of assessments variable across funders and researchers
- Compounds moving to clinic despite non compelling preclinical data leading to (predictable) failure in the clinic
- Often lacking realistic development perspective- limited industry participation
- Multiple compounds to go into clinic- limited number of patients

*Sophisticated diligence process beyond the abilities of typical academic advisory committee*

*Resulting in greatly increased credibility with non profit, industry and VC funders*
TACT Review Process

- Completed Application Form Submitted
- Meeting Convened
- General Non-confidential Report

- 3 months - 2.5 months 0 + 1.5 months + 2 months

Confirmation of compounds for review and feedback to ALL applicants (re: proposal to be reviewed or not)

Report to Applicant (and Sponsor, Funders & PI as applicable)
How We Work with TACT

- We use the same application forms
- We require grantees to undergo TACT review as a condition of funding
- Fund and attend review meetings
- We may modify our grant requirements as a result of the TACT review

Benefits of Working With TACT

- More extensive access to experts than we could develop on our own
- Reduces burden on reviewers and applicants because centralized process can be shared among multiple groups
TACT-PPMD Partnership Opportunities

Researchers
• Unique, multidisciplinary, review by disease and development experts
• Informed and credible program
• More likely to get funded
• Enables cross talk with industry
• Training of young investigators

Patient organizations
• Comprehensive objective assessment - raise the bar
• Increase odds of clinical success
• Avoid duplication

- Highly educational to academic researchers on realities of drug development
- Can be exported to other rare disease
Unique Initiative for Advancing Therapeutics for Rare Diseases

April 2013

www.CydanCo.com
Cydan Launches Venture Backing for Drug De-Risking Accelerator
Cydan LLC of Cambridge announced its launch with $16 million in financing.

Cydan Hopes To Accelerate Rare Disease Drug Development With $16 M Raise
By Lisa LaMotta
Posted: April 11 2013 1:00 AM

Newco Cydan raises $16M for Orphan drugs
April 11, 2013
Cydan LLC (Cambridge, Mass.) debuted on Thursday with $16 million in an undisclosed venture round co-led by New Enterprise Associates and Pfizer Venture Investments. Alexandria Real Estate Equities also participated. Cydan is aiming to identify and de-risk assets across all rare disease areas, with the goal of spinning out the most viable programs into newcos. The company plans to spin out its first newco next year.

Pfizer Ventures backs effort to amp up orphan-drug development
April 11, 2013 | By Tracy Staton

David Mott, ex-CEO of MedImmune and a high-profile biotech partner at New Enterprise Associates, has led the way toward an orphan drug accelerator also backed by Pfizer Ventures. The Cambridge, MA-based effort, dubbed Cydan, will scout out promising early-stage assets and mold them into pipeline programs for eventual spin-out into new biotech companies.
Cydan Accelerator: Sourcing to Spin-Out

- **Ongoing surveillance** of rare disease landscape
- **Diligence** on those that fit profile
- **De-risk**
  - Advance those meeting diligence criteria
  - Predetermined milestone for go/no-go decision to NewCo

Up to 5 Spin-outs in 4 years
Flexible Model allows for Diverse Collaborations

Patient Organizations
- Advocacy groups play key role in rare diseases

Academia
- Academia often at forefront of new genetic discoveries in rare diseases

Industry
- Large pharma and small biotech
- Deprioritized or under-resourced projects, new applications of technology

NIH / Consortia
- Unprecedented NIH efforts to work across divisions and with industry
Patient Registries Critical

*Registries represent a means to execute clinical studies, as well as to validate market size*

- Build the Key Opinion Leader community globally
- Uniform and reliable diagnosis
- Confirm incidence and prevalence of disease
- Establish the natural history of disease
- Provide comprehensive data for clinical research and for regulatory purposes, e.g. post-approval commitments
- Connect patient association/families to research and clinical trials
- Promote improved diagnosis and medical care
- An important element of diligence of opportunities

*Rising number of patient registries across rare disease indications*
Key points

• Successful integration of all industry and non-profit key stakeholders is a must have

• No experiments in isolation

• Most informed to clinic not 1\textsuperscript{st} to clinic

• High clinical impact is the focus

Thank you!