Unique Challenges of Clinical Development for Emerging (Rare Disease) Therapies

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Abeona Therapeutics Inc.
Rare Disease Therapy Goals: Helping Kids Develop Superpowers

- Get bitten by genetically modified spider
- Be immersed in toxic sludge
- Exposure to cosmic radiation
- Imbibe chemical superformula
- Inherit X gene

All modify the human genome – but not recommended
Through the looking glass...

History of Abeona Therapeutics

• Initially a Private company founded in 2013
  – Challenge: spinning out of academic institution
    • License terms
    • Required additional licenses

• Seed round of $750,000
  – Challenge: where to use $$ for the most value-drivers

• $5M Series A round led by MPS foundations
  – Challenge: $$ for drug manufacture, getting into clinical trials

• Public company merger in 2015 – different issues
  – Challenge: Reverse merger – not typical market entry
    • Educating investors
    • Pipeline expansion
<table>
<thead>
<tr>
<th>Gene Therapies</th>
<th>Research</th>
<th>Preclinical</th>
<th>Phase I/II</th>
<th>Marketed</th>
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</thead>
<tbody>
<tr>
<td><strong>Metabolic</strong></td>
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<tr>
<td>ABO-102 (scAAV-SGSH)</td>
<td>Sanfilippo syndrome Type A (MPS IIIA)</td>
<td>✔️ ✔️ ✔️ ✔️</td>
<td>✔️ ✔️ ✔️ ✔️</td>
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<tr>
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<td>ABO-201 (scAAV-CLN3)</td>
<td>Juvenile Batten disease (CLN3)</td>
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<tr>
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<td>Infantile Batten disease (CLN1)</td>
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<td>✔️ ✔️ ✔️ ✔️</td>
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<td><strong>Dermatology</strong></td>
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<tr>
<td>EB-101 (LZRSE-Col7A1)</td>
<td>Recessive dystrophic epidermolysis bullosa (RDEB)</td>
<td>✔️ ✔️ ✔️ ✔️</td>
<td>✔️ ✔️ ✔️ ✔️</td>
<td>★</td>
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<tr>
<td>EB-201 (AAV DJCol7A1)</td>
<td>Epidermolysis bullosa (EB)</td>
<td>✔️ ✔️ ✔️ ✔️</td>
<td>✔️ ✔️ ✔️ ✔️</td>
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<td><strong>Hematology</strong></td>
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<td>ABO-301 (AAV-FANCC)</td>
<td>Fanconi anemia (FA)</td>
<td>✔️ ✔️ ✔️ ✔️</td>
<td>✔️ ✔️ ✔️ ✔️</td>
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<tr>
<td>ABO-302 (CRISPR-Cas9)</td>
<td>Rare blood diseases</td>
<td>✔️ ✔️ ✔️ ✔️</td>
<td>✔️ ✔️ ✔️ ✔️</td>
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**AAV Vector Platform**

| AIM<sup>®</sup> Vectors | 2nd Gen and New AAV Products |

- ✔️ Orphan Drug Designation (FDA)
- ✔️ Orphan Drug Designation (EU)
- ✔️ Rare Pediatric Disease Designation (FDA)
- ✔️ Fast Track Designation (FDA)
- ★ Breakthrough Therapy Designation (FDA)
Global Foundations and Family Support
Working together to climb higher

Inside Mt. Rainier Crater at Summit 14,440 ft

2016 Mt. Rainier Summit
- Awareness Campaign
- Fundraiser
- MPS III Family member
- Foundation
- Abeona
What’s in a sneeze?

CMC Challenges in Gene Therapy Manufacturing in 2014-2017

• If one person sneezed... how much virus is needed?
• Who is going to make it? - Lack of qualified vendors
• Process is challenging and with low yields/scale-up concerns
• Proper planning for early phase trials
  – Process development and transition to late/commercial needs while balancing investments and going on little info
• Assays of the appropriate method/qualification/certification
• Hasn’t really changed in 2017....
Who’s on first?

Team Challenges: Building A Bench of Rare Disease Team Members

• Expertise/experience is not abundant, make it work through virtual team while building the nexus
  – Consultants and KOLs are critical for early stage development
• Identifying appropriate external resources to help keep team focused with programs progressing
  – Foundation, Incubator and grant support
• Maintain ability to remain up to date on a changing regulatory, legislative environment
• Building a center of gravity in a virtual world
Education is key

Regulator Challenges: Bring everyone along on the journey

• Time/effort required to educate (due to rare disease, emerging therapy)
• Patient groups/caregivers/individuals require repeated and different approaches to demystifying gene therapy, drug development
• Specifically, the move from private to public and timing with the change from pre-clinical to clinical and ability to share info directly with foundations
• FDA needs education on specific rare disease
  – RDEB wounds are not like diabetic ulcers
  – MPS IIIA and IIIB are most definitely pediatric diseases
  – Education on ultrarare diseases combined with the difference of developing a novel/emerging therapy vs. traditional small mol.
• Payers will fall into this category as well
Future Challenges in Translation: Pricing

HOW DO WE MAKE SUPERHEROES A REALITY?..... AND HOW TO WE PRICE THEM?
Gene Therapy Treatment Outcome Paradigms

- Normal Development
- Disease stabilization
- Disease Reversal
- Disease Onset Delay
- Disease attenuation

Age (years)

Development Score

- Subjects in late disease
- Subjects in early disease
Setting expectations – current cost of treating rare disease patients

### Costs per patient of managing selected disorders

These approximate estimates are drawn from references (10–13). CFTR, cystic fibrosis transmembrane conductance regulator.

<table>
<thead>
<tr>
<th>DISEASE ENTITY</th>
<th>MANAGEMENT PLAN</th>
<th>~COST/YEAR ($)</th>
<th>~COST/LIFETIME ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis</td>
<td>General support</td>
<td>25,000</td>
<td>750,000</td>
</tr>
<tr>
<td></td>
<td>Drug to enhance CFTR function (Kalydeco)</td>
<td>300,000</td>
<td>5,000,000</td>
</tr>
<tr>
<td>Gaucher disease</td>
<td>Regular enzyme replacement</td>
<td>200,000</td>
<td>5,000,000</td>
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<tr>
<td>Hemophilia A</td>
<td>Prophylactic or periodic factor administration</td>
<td>300,000</td>
<td>5,000,000–10,000,000</td>
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<tr>
<td>Sickle cell disease</td>
<td>General medical support and hydroxyurea as standard of care</td>
<td>25,000</td>
<td>1,000,000</td>
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<tr>
<td>Recessive dystrophic Epidermolysis bullosa</td>
<td>Bandages, ointments, pain</td>
<td>$227 - $670/day</td>
<td>$7,300,000</td>
</tr>
</tbody>
</table>

*Sources: Orkin and Reilly, Science, 2016  
Kirkorian, Ped. Derm., 2013*
Question: How would you describe your (insurance) company’s posture toward the coming wave of orphan drugs?

- No, it is not on our corporate agenda at this time
- No, we think it is important, but are unsure what to do
- No, but we are in dialogue with providers and physicians now about this
- Yes, strategic plans are in process but have not yet been rolled out
- Yes, we have a plan that is being actively rolled out at the current time

DRGs? 340B exclusion? Inpatient/Outpatient? How are these categorized?

Ref: Hanfield, 2013. Am. Health drug benefits; 6(9)
Organ Transplants are Viewed as Most Direct Comparable to Gene Therapy Treatments

Organ transplants:
- Can cost $1M/patient
- One time intervention

Source: Access Insights, 2015
Considerations for Pricing Models

• Should a blood disorder with a plasma biomarker be reimbursed similar to:
  – A CNS disease?
  – A muscular dystrophy?

• How should reimbursement be valued in patients at different stages of disease?

• How will retreatment or availability of new treatments be factored?

• What if patient dies of disease progression?

• Switching health care providers and pre-existing condition.....
2018 – Working Together to Climb Higher!

New challenges, new goals = more chances to succeed
Thanks!

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