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

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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**

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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

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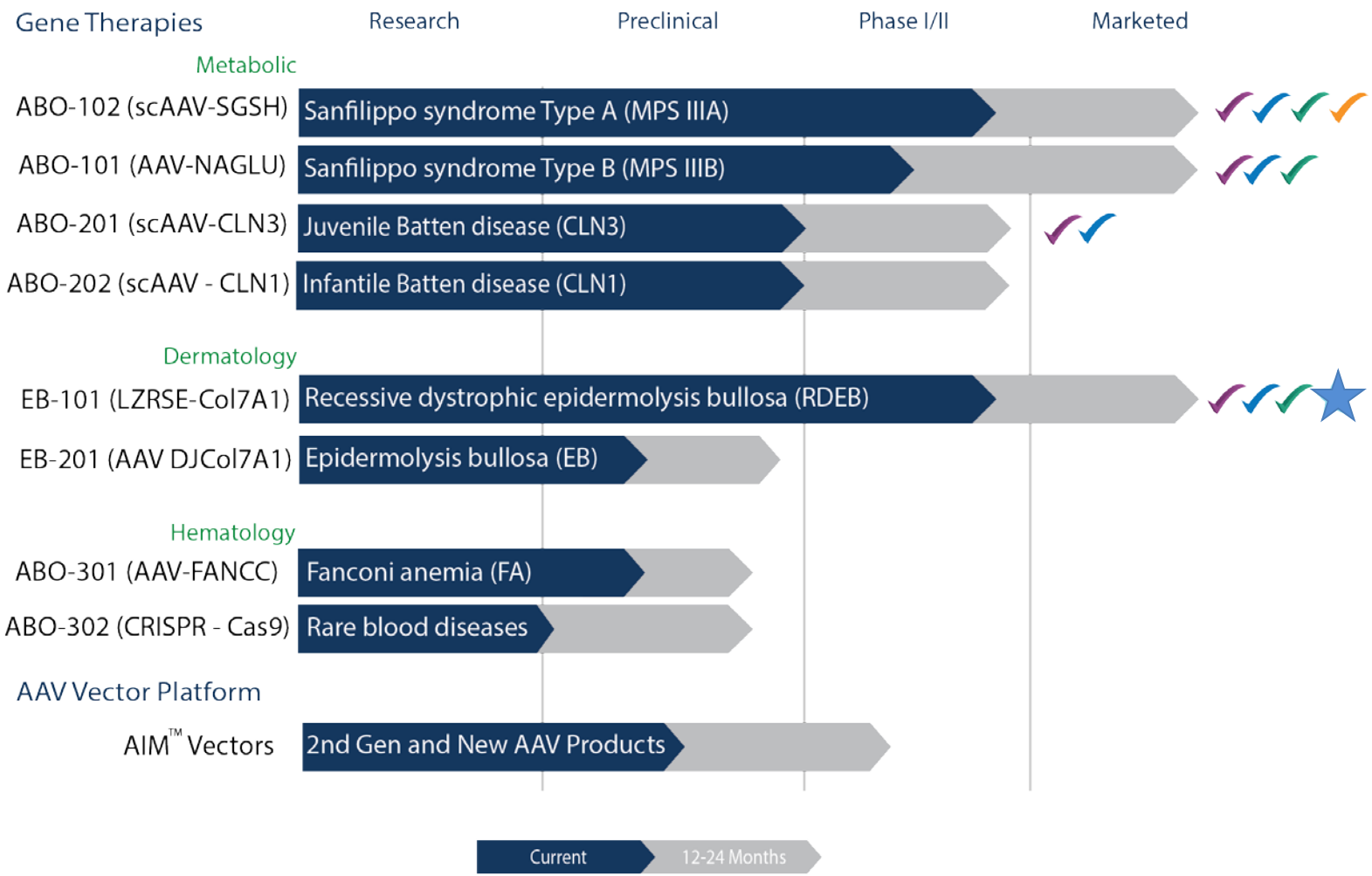
Abeona Gene Therapy Pipeline



Global Foundations and Family Support

★ Original Founding Foundations

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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**

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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?

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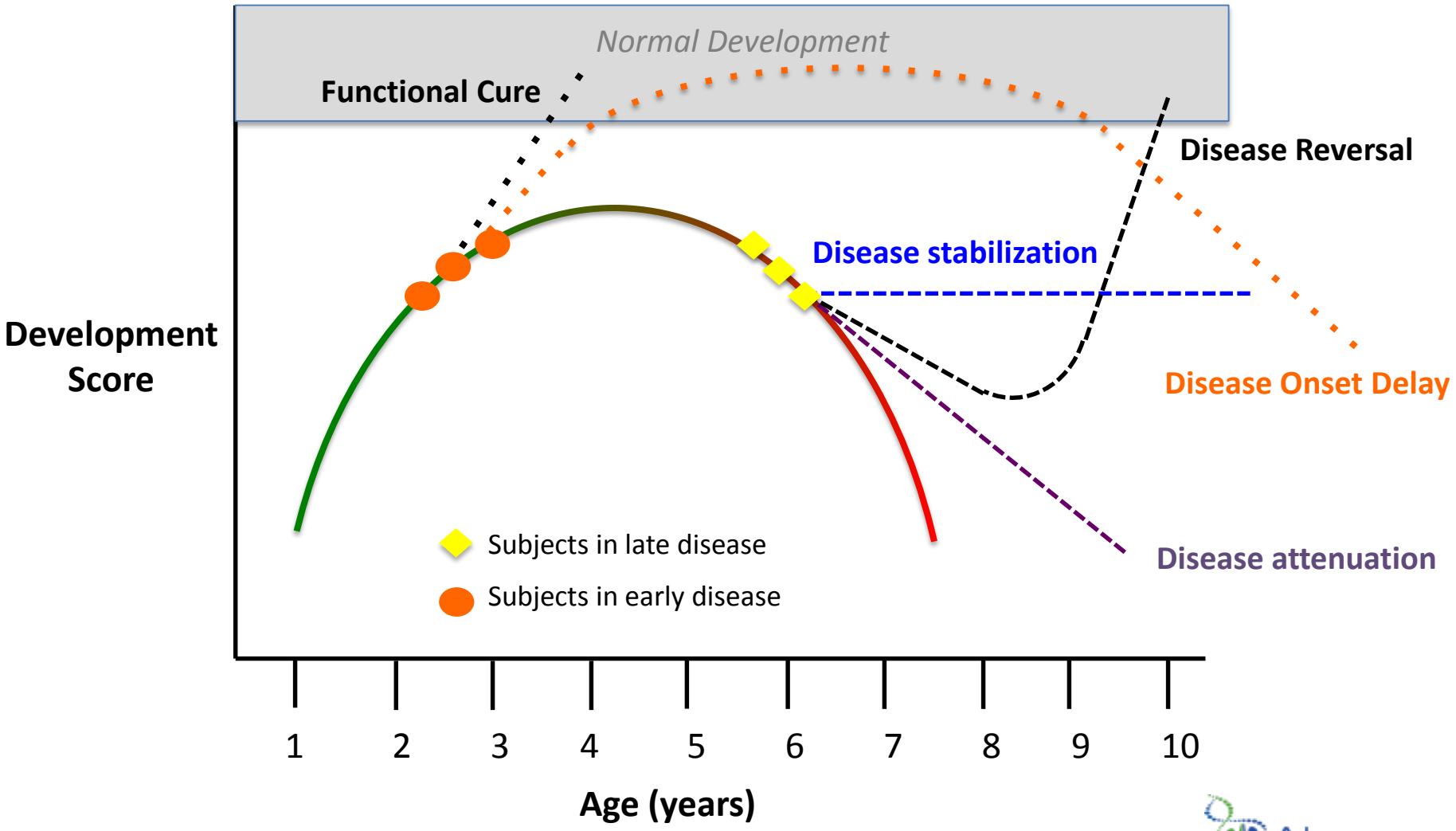
Gene Therapy Treatment Outcome Paradigms



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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.

DISEASE ENTITY	MANAGEMENT PLAN	~COST/YEAR ($)	~COST/LIFETIME ($)
Cystic fibrosis	General support	25,000	750,000
	Drug to enhance CFTR function (Kalydeco)	300,000	5,000,000
Gaucher disease	Regular enzyme replacement	200,000	5,000,000
Hemophilia A	Prophylactic or periodic factor administration	300,000	5,000,000–10,000,000
Sickle cell disease	General medical support and hydroxyurea as standard of care	25,000	1,000,000
Recessive dystrophic Epidermolysis bullosa	Bandages, ointments, pain	$227 - $670/day ~ $250,000/year	$7,300,000

Sources: Orkin and Reilly, Science, 2016
Kirkorian, Ped. Derm., 2013

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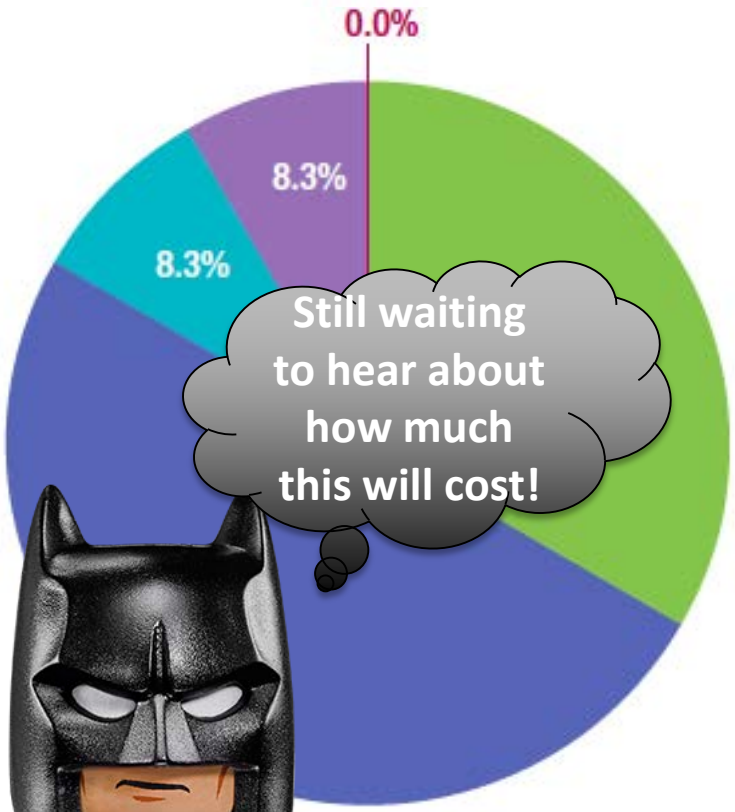
Insurance Company Concern Towards Orphan Drugs

Question asked: 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)*

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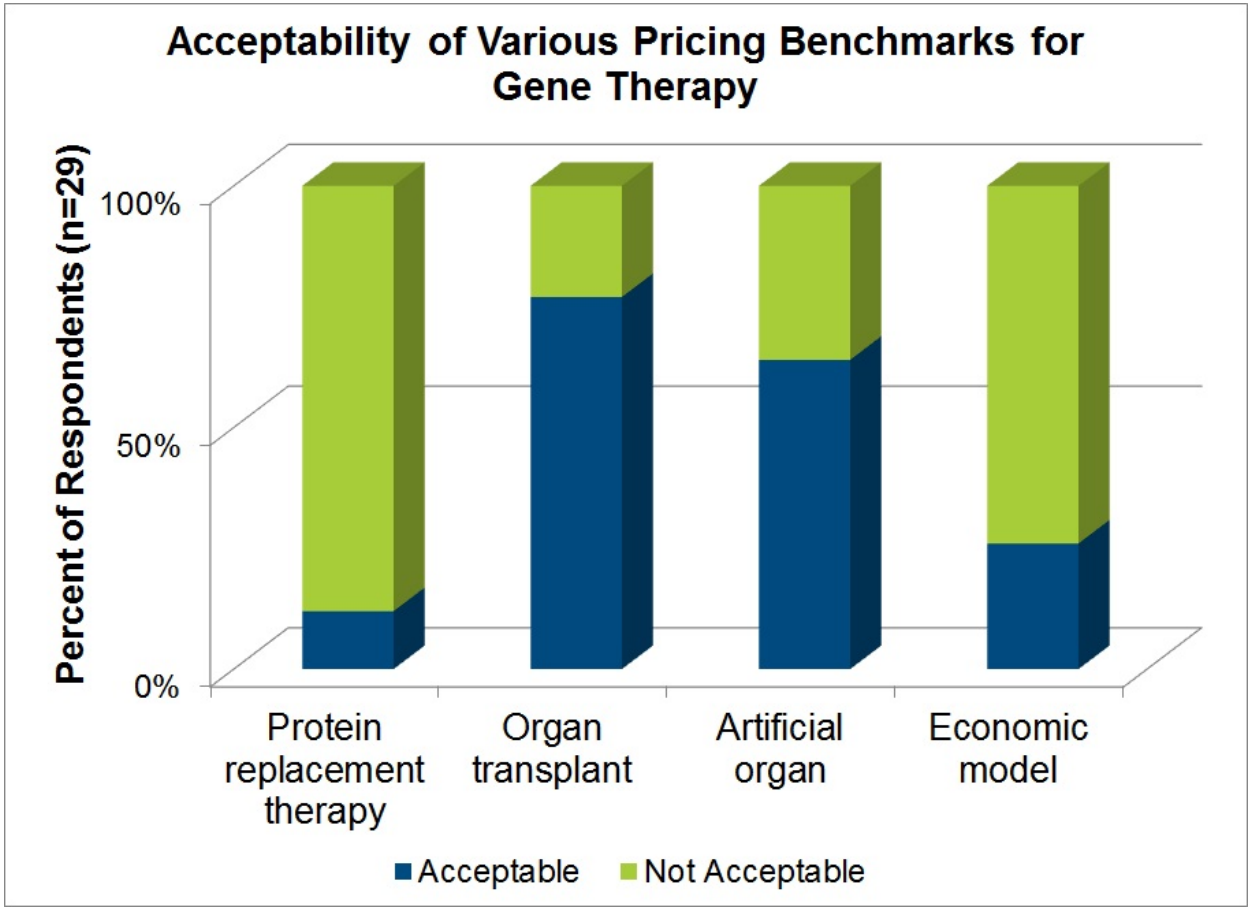
Organ Transplants are Viewed as Most Direct Comparable to Gene Therapy Treatments



Organ transplants:

- Can cost $1M/patient
- One time intervention

Source: Access Insights, 2015

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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

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Thanks!

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