Investment and Collaboration to Realize the Promise of Gene Therapy

Elizabeth White, Ph.D.
Asst. Vice President, Commercial Development, Rare Disease and Gene Therapy

Gene Therapy for Rare Disorders 2017
April 26, 2017
Agenda – Realizing the Promise of Gene Therapy

- Pfizer’s Gene Therapy Strategy
- State of the Industry and Prospects for the Future
- Risks and Challenges
- Collaboration and Partnerships Across the Continuum Are Critical for Success!
Agenda – Realizing the Promise of Gene Therapy

- Pfizer’s Gene Therapy Strategy
- State of the Industry and Prospects for the Future
- Risks and Challenges
- Collaboration and Partnerships Across the Continuum Are Critical for Success!
Pfizer’s Gene Therapy Strategy and Vision

We aspire to be a LEADER IN GENE THERAPY and a PARTNER OF CHOICE

Transformational Portfolio & Capabilities

- Proprietary rAAV platform
- Clinical stage portfolio
- Rare disease R&D, regulatory & commercial expertise

Scalable Manufacturing

- GMP Vector Core Facility
- Proprietary cell lines
- Sophisticated vector analytics
- Commercial manufacturing investments
Agenda – Realizing the Promise of Gene Therapy

- Pfizer’s Gene Therapy Strategy
- State of the Industry and Prospects for the Future
- Risks and Challenges
- Collaboration and Partnerships Across the Continuum Are Critical for Success!
Investment and Partnering in Gene Therapy Continues to Flourish

- Many deals and strategic alliances
  - Industry-industry and industry-academia

- Recent examples include:
  - Sanofi/Genzyme and Voyager collaboration
  - Pfizer acquisition of Bamboo Therapeutics
  - Avexis IPO
  - Biogen and Univ. of Pennsylvania collaboration
  - Audentes IPO
  - Bluebird Bio and Lonza manufacturing agreement
Technology and Regulatory Science Advancing, Leading to Gene Therapy Pipeline Progress

• 21st Century Cures Act – provisions aimed at expediting approvals

• EMA Action Plan providing regulatory and scientific support for Advance Therapy Medicinal Products (ATMPs)

• GSK’s *ex vivo* gene therapy Strimvelis gained European Marketing Authorization

• Spark Therapeutics rolling BLA submission for IRD gene therapy

• Hemophilia Gene Therapy programs continue to progress
Promising Gene Therapy Pipeline Should Deliver Important Medicine Approvals Over the Next 8-10 Years…

<table>
<thead>
<tr>
<th>Development Phase</th>
<th>Number of Gene Therapy Clinical Trials¹</th>
<th>Probability of Success to Approval²</th>
<th>Projected Approvals in Next 8-10 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>161</td>
<td>8%</td>
<td>13</td>
</tr>
<tr>
<td>Phase II</td>
<td>233</td>
<td>16%</td>
<td>37</td>
</tr>
<tr>
<td>Phase III</td>
<td>31</td>
<td>45%</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>425</td>
<td></td>
<td>64</td>
</tr>
</tbody>
</table>

But Perhaps Not the “Tsunami” That Is Sometimes Projected!

¹Alliance for Regenerative Medicine 2016 Annual Data Report (Gene Therapy and Gene-Modified Cell Therapy)
²Pfizer Analysis for Rare Disease
Agenda – Realizing the Promise of Gene Therapy

• Pfizer’s Gene Therapy Strategy
• State of the Industry and Prospects for the Future
• Risks and Challenges
• Collaboration and Partnerships Across the Continuum Are Critical for Success!
For Success in Gene Therapy, Four Key Areas Need Simultaneous and Coordinated Advancement

- Suitable tissue targeting
- Corrective transgene optimization
- AAV immuno-biology
- Vector analytics
- Next-Generation process technology
- Phase 1/2 manufacturing at disease specific scale
- Process analytics and standards
- Large-scale commercial manufacturing
- Innovative clinical development paradigms
- Advancements in regulatory science
- Global regulatory harmonization
- Management of commercial model disruption
- Innovative market access models
- Definition of market exclusivity
- Collaborative payer and policy solutions
Two Types of Immune Response Pose Challenges in AAV Gene Therapy

Not all patients are eligible for AAV therapy due to pre-existing neutralizing antibodies:

- Previous natural exposure to AAV generates antibodies
- Treatment can also generate antibodies: cannot dose again
- Antibodies eliminate dosed vector from circulation prior to delivery to target cells
- Antibodies make ~40% patients ineligible for therapy

Solution
- Screen for antibodies prior to therapy
- Develop technologies to overcome

Delivering gene therapy may elicit a primary immune response

- Delayed immune reaction to viral gene therapy 4-12 weeks post-dose
- T-cell mediated response destroys treated cells

Solution
Prevent or manage with steroid or other immunosuppressive therapy
Gene Therapy Manufacturing Capabilities - Scarce in the Industry

Very Wide Dose Ranges May Be Needed Depending on Target Tissue

**Projected Dose:**
- Local Eye: $\sim 1 \times 10^{11} \text{ vg (✓)}$
- Local Brain: $\sim 1 \times 10^{12} \text{ vg (✓)}$
- Systemic Liver: $\sim 1 \times 10^{14} \text{ vg (±)}$
- Musculoskeletal: $\sim 1 \times 10^{15} \text{ vg (⁇)}$
Hemophilia GTx Introduction will be Disruptive to the Current Treatment Paradigm, Distribution, Pricing, and Reimbursement
Gene Therapy Presents Challenges to Current Payment Models
- Key Uncertainties Identified by Payers

- **Affordability / Budget Impact**
  - Clinical benefit will be key consideration when payers evaluate gene therapies
  - Payers recognize the potential of gene therapies to impact patients’ QOL
  - Successful access and adoption requires changes to current payment models

- **Durability of Effect**

- **Patient Migration Across Plans**
## Multiple Payment Models Under Consideration to Enable Patient Access to Gene Therapy Medicines

<table>
<thead>
<tr>
<th>Potential Payment Models</th>
<th>Ability for Model to Address Key Concerns</th>
<th>Operational Feasibility under current US system</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Budget Impact/Affordability</td>
<td>Benefit Duration Uncertainty</td>
</tr>
<tr>
<td>Lump-Sum</td>
<td>❌</td>
<td>❌</td>
</tr>
<tr>
<td>Reinsurance/Pooled risk</td>
<td>✓</td>
<td>❌</td>
</tr>
<tr>
<td>Reinsurance/Pooled risk with performance guarantee</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Periodic payment</td>
<td>✓</td>
<td>❌</td>
</tr>
<tr>
<td>Periodic payment with performance guarantee</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Expect a variety of payment models, customized to the particular gene therapy, payer archetype and healthcare system – **ONE SIZE DOES NOT FIT ALL!!**
Agenda – Realizing the Promise of Gene Therapy

• Pfizer’s Gene Therapy Strategy
• State of the Industry and Prospects for the Future
• Risks and Challenges
• Collaboration and Partnerships Across the Continuum Are Critical for Success!
Pfizer Internal Capability Build Complimented by Multiple Collaborations and Acquisitions
Shaping the Environment: Asset and Macro Considerations

Gene Therapy Market Evaluation and Shaping Activities

Asset-Specific Activities
- Payor Ad Boards
- Patient Ad Boards
- Existing preconceptions
- Alternative treatments

Gene Therapy Category Activities
- Regulatory policy
- Access & reimbursement rules
- Willingness to pay
- Policy Fora
- Educational Events
- Other company actions
- Policy-making body perspectives
- Existing preconceptions
- Government financial pressures

Existing preconceptions
Opportunities for Gene Therapy Policy Advocacy Engagement

ARM promotes legislative, regulatory, reimbursement, investment, technical and other initiatives to accelerate the development of safe and effective regenerative medicine technologies. ARM also works to increase public understanding of the field and its potential to transform human healthcare.

**Working Groups:**
- Regulatory
- Government Affairs
- Access & Reimbursement

**Conferences:**
- Advanced Therapies Summit - March
- Cell & Gene Exchange – May 22nd
- Legislative Fly-In – May 23rd
- Meeting on the Mesa – October 4th

---

**The Forum on Regenerative Medicine – Gene Therapy Policy Workshop**

The Forum identifies potential barriers to scientific and therapeutic advances, examines the impact of current policies and discusses opportunities to facilitate more effective partnerships among key stakeholders.

The GT Policy workshop will be held in October to discuss scientific, policy and implementation issues for gene therapy.

---

**Genetic Alliance Think Tank**

Genetic Alliance transforms the healthcare system and engages consumers to reclaim their own health.

The Industry Think Tank is a flexible mechanism bringing stakeholders together to inform one another about diverse perspectives, devise experiments that can test potential solutions, leverage our decades of partnerships with industry and catalyze relationships and programs to achieve better outcomes.
Critical to Plan Early and Collaborate Across All Stakeholders to Prepare the Market for Transformative Therapies

The value of transformative therapy is clear:
• One-time treatment with potential for “cure,” offsetting medical costs
• Potential for targeted therapies where none exist for difficult genetic diseases
• Greatly improved quality of life for patients

Technical, manufacturing & clinical development progress must be nurtured:
• Collaborations and investment of all types needed to make the most of quickly advancing science and technology, and to develop the right standards
• Industry - academia - regulators

Stakeholder collaboration needed to insure access to gene therapy medicines:
• Management of disruption to medical business models
• Payment and financing challenges and uncertainties
• Regulatory and policy advancements needed to keep up with innovations
• Patient voice is critical!

Realizing the promise of gene therapy:
• Take a proactive approach to partnering with various stakeholders
• We all need to work together and move in the same direction
• Coalition building, development of common language, and education of all stakeholders is key!