Moving from Chronic Therapies to Cures

Policy Solutions to Facilitate Access
Francesca Cook
Moving from Chronic to Cure – The Promise of Gene Therapy

**Gene Therapy**
- Addresses underlying cause of disease
- One-time administration
- Cure or transformative

**Early Experience (EU)**
- Glybera
  - 1 patient
  - Pulled from market
- Strimvelis
  - 1 center in Milan
  - 2 patients
  - GSK divesting RD portfolio

**Next Wave**
- US 1st approval; more to follow
  - Novartis CAR-T
  - Next up: Spark, Kite
- Over 9001 gene therapy trials; 752 in PhIII
  - Promising early data
    - Hemophilia
    - SMA

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1,2ARM 2017 Q2 Analysis,
Insights From Evolution Therapeutic Antibody And Orphan Drug Markets

Inflection point came almost a decade after first approval, driven by advancements in science, manufacturing … and at least one recognizable commercial success

- Orthoclone (1986) is not commercially successful
- Technical challenges (immunogenicity, production) hinder field growth
- First blockbuster
- Humanized Ab + CHO cell mfg drive progress
- Global market worth $95B (2017E)
- 60+ products, 300+ pipeline
- Clinical POS ~26%

- Only 38 drugs approved for rare diseases prior to Orphan Drug Act (1983)
- ODA provides commercial incentives
- First successful ultra-orphan, creation of a new business model
- Global market worth $125B (2017E)
- 400+ products, 800+ pipeline
- Clinical POS ~25%

Gene therapy field may not be derailed if first products are not commercially successful, but we need to find the right products and models for long-term growth and sustainability
What is fundamentally different about gene therapy?

Gene and cell therapies are unique in many different ways and require thoughtful commercial planning by innovators and payers

<table>
<thead>
<tr>
<th>Product Attributes</th>
<th>Commercial Implications</th>
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</table>
| **Curative potential** | ▪ High clinical and economic value  
▪ Broader societal benefits  
▪ Potential for portfolio effect and/or surge adoption at approval |
| – Targeting underlying biology  
– Dramatic magnitude of effect  
– Impact on quantity and quality of life | |
| **“One and done”** | ▪ Long-term clinical uncertainty at approval  
▪ Higher one-time price  
▪ Potentially easier uptake outside major markets |
| – Single or acute administration vs chronic  
– Repeat administration may not be feasible  
– Irreversible procedure | |
| **Product complexity** | ▪ Need for more product education  
▪ Need for specialized COEs & high-touch training  
▪ Need to identify and mature supply chain  
▪ High initial COGS |
| – Viral manufacturing  
– Autologous cell processing  
– Specific route-of-administration | |
The proliferation of expensive ‘curative’ therapies comes at a time when healthcare systems are already facing financial challenges

Insurers/HTAs are already struggling to afford pricey therapies and efforts to restrain rising drug costs are increasing.

- Payers/HTAs are taking steps to limit the budgetary impact of expensive new drugs:
  - Utilization management
  - Value-based reimbursement/risk sharing
  - Enhanced orphan drug scrutiny
  - Increased patient OOPs
- The Sovaldi experience is still fresh and payers are nervous about the impact of gene and cell therapies

**Specialty drug costs are growing even faster...**

- In 2015 specialty drugs were used by 1-2 percent of the population but accounted for 38% of total drug expenditures
- Number of people with annual drug costs >$50K increased 63% in 2014
- [http://www.pewtrusts.org/~media/assets/2016/12/specialty_drugs_and_health_care_costs.pdf](http://www.pewtrusts.org/~media/assets/2016/12/specialty_drugs_and_health_care_costs.pdf)
Consequently, broad adoption of gene and cell therapies will require overcoming key challenges and thinking differently

- Moving from “chronic” to “cure” can transform the healthcare system but..
  - GTx is new and untested
  - Healthcare system not set up for curative therapies

- Two key factors will impact GTx adoption:
  - Uncertainty
    - Duration
    - Safety
  - Affordability
    - Higher pricing (orphan)
    - Surge potential (blockbuster)

Overcoming uncertainty and affordability barriers is critical to facilitate GTx adoption, ensure patient access, and support continued innovation
Consensus is building around payment and financing models to address uncertainty and affordability.

**Uncertainty**

- New payment models to spread/share risk

**Affordability**

- Financing models to limit exposure (payer)—avoid “solvaldi effect” and help patient and families access cures

**Potential Solutions**

- Payments over time (Annuities)
- Pay for Performance or Value Based Arrangements (VBA)

- Reinsurance/Stop Loss
- Risk Pools
- Co-pay reform
- Healthcare consumer loans

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**Payer focused**

**Patient focused**
# Summary of Payment and Financing Solutions

<table>
<thead>
<tr>
<th>Alt payment models</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td><strong>Annuity</strong></td>
<td>Payment spread over a pre-specified period (e.g. monthly or set number of years)</td>
</tr>
<tr>
<td><strong>VBA</strong></td>
<td>Payment adjusted based on pre-agreed health care outcomes, adjustments could take the form of a rebate or payback and/or be tied to an annuity or up front payment arrangement.</td>
</tr>
</tbody>
</table>

| Financing Models   | |
|--------------------| |
| **Reinsurance/stop loss** | Financial arrangements that limit insurer/institution exposure to the risk of unexpected price or volume thresholds of high-cost cases (individuals) |
| **Risk Pools**     | Similar to reinsurance, a dedicated fund (can be sponsored by the government, insurers or potentially manufacturers) to cover healthcare costs associated with high cost cases. Specific funds could be set up to support curative therapies |

| Patient OOP Support | |
|--------------------| |
| **Co-pay reform**  | Would enable coverage of out of pocket (OOP) expenses for travel, lodging and other expenses not traditionally covered, but can be critical for families requiring highly specialized treatment at COEs |
| **HC consumer loans** | Mortgage or credit care-like financing provided by financial intermediaries (could include manufacturers) to enable low-interest loans to families to cover high OOP costs (co-pays, co-insurance, and potentially cures themselves) |
While annuity payments are a relatively new concept, several of the other mechanisms to overcome payment and financing barriers have been used previously and are not specific to gene and cell therapies.

<table>
<thead>
<tr>
<th>Alt Payment Models</th>
<th>Financing Options</th>
<th>Patient OOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annuities</td>
<td>VBA</td>
<td>Reinsurance/Stop Loss</td>
</tr>
<tr>
<td>New</td>
<td>✓</td>
<td>✓*</td>
</tr>
<tr>
<td>Exists today</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Model Applicability to GTx vs. other types of therapies**

| GTx                  | ✓                          | ✓                     | ✓          | ✓*             | ✓                   | ✓                   |
| Chronic therapies    | ✓                          | ✓                     | ✓          |                | ✓                   |                     |

*Risk pools were common pre-ACA, it is envisioned that risk pools specific to curative therapies/GTx could be created.

New models needed for curative therapies
Value Based Arrangements are gaining more traction in the U.S.

| VBAs |
|------------------|------------------|
| Therapy          | Repatha          | Kymriah          |
| Product Type     | PCSK9 inhibitor  | Gene-based cell therapy |
| Indication       | HeFH/CVD         | Pediatric B-cell acute lymphoblastic leukemia |
| Manufacturer/Payer agreement | Amgen/Harvard Pilgrim | Novartis/CMS |
| VBA Characteristics | • LDL-lowering targets  
|                  | • Payback (payer and patient) if targets not met  
|                  | • Price protection (no increases)  
|                  | • Preferred status | • Payment only if patient responds by end of one month  
|                  |                  | • Similar agreement expected with other payers |

Key factors for VBAs – 1) clinical outcome metrics for success easily identifiable and 2) success is evident within a short timeframe

Kymriah’s approval showcased new engagement by the U.S. Center for Medicare and Medicaid Services (CMS) in outcomes based payment.

- CMS lauded the development of Kymriah and committed to modernizing current healthcare payment systems and exploring innovative pricing models:

  “Through the authority provided to the Center for Medicare and Medicaid Innovation (CMMI), CMS will aim to identify and alleviate regulatory barriers in Medicare and Medicaid as may be necessary to test payment and service delivery models that involve value-based payment arrangements.”
Implementing new models and thinking differently will take a village

Gene/Cell Therapy Multi-Stakeholder Dialogue

- Patients, Families, and Advocacy Organizations
- Physicians, Hospital Systems, & Med Societies
- Policy Makers
- Financial Intermediaries
- Innovators
- Industry Trade Organizations
- Regulatory Agencies
- Payers & Health Tech Assessment Orgs
A number of entities are advancing thinking around alternative models

<table>
<thead>
<tr>
<th>Organization</th>
<th>Focus / Membership</th>
<th>Value Frameworks</th>
<th>Alt Reimb</th>
<th>Alt Financing</th>
<th>Legal Barriers to New Models</th>
<th>Patient Access</th>
<th>CoE Model</th>
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<tr>
<td>Alliance</td>
<td>Policy, Education, Access Regenerative medicine companies</td>
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<td>✓</td>
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<tr>
<td>MIT NEW DIGS</td>
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<tr>
<td>Bio</td>
<td>Alternative Financing Biopharma, payers, providers</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>ICER</td>
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<tr>
<td>Duke</td>
<td>Alternative Financing Biopharma, payers, providers</td>
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<tr>
<td>Marquis</td>
<td>Value, quality, patient access HSCT COEs, payers, re-finance co</td>
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<tr>
<td>NMDP</td>
<td>Education, Policy Regen med scientists, clinicians, companies and patients</td>
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<td>eunethta</td>
<td>HTA methodology and guidance EU HTA Network</td>
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Consortia activities are moving from identification of new models to solution generation

<table>
<thead>
<tr>
<th>Organization</th>
<th>Key 2017-2018 Activities</th>
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| **ALLIANCE** | Reimbursement Committee White Papers Series  
|              | NAMCP partnership  
|              | Meeting on the Mesa |
| **MITNEWDIGS** | Financing Cures in the U.S. (FoCUS) initiative  
|              | Assessment oncology and gene therapy case studies |
| **Bio** | Curative Therapies Working Group  
|          | Exploring VBA pilots and logistics with HHS/CMS |
| **ICER** | Gene Therapy Summit, Orphan Therapy Summit (2016-17)  
|          | Assessments on Luxturna & CAR-Ts planned for early 2018 |
| **Duke** | Four white papers on VBAs (2017)  
|          | Exploring potential pilots (2018) |
| **National Marrow Donor Program** | Recent contact limited, main focus is on cell therapies  
|          | Insight on COE, re-finance, patient OOP reform still relevant |
| **American Society of Gene and Cell Therapy** | Annual pre-ASGCT commercialization workshop  
| **NORD** | Co-pay reform, protect patient rights under ACA |
Global regulators also have adopted mechanisms to accelerate advanced therapies

<table>
<thead>
<tr>
<th>Regenerative Therapy Policies by Geography</th>
<th>Accelerated Review</th>
<th>Accelerated Approval</th>
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<tbody>
<tr>
<td>US</td>
<td>Regenerative Medicine Advanced Therapy Designation</td>
<td>√</td>
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<tr>
<td>EU</td>
<td>Advanced therapy</td>
<td>√</td>
</tr>
<tr>
<td>Japan</td>
<td>2014 Safety of Regenerative Medicines legislation Sakigake and Conditional approval</td>
<td>√</td>
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Reasons for optimism

- Engagement opportunities exist

- U.S. Regulators becoming more involved

- Consortia moving the needle on thinking through payment and financing challenges