The Relevance of Global Convergence to Accelerating the Availability of Gene Therapies

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ASGCT Policy Summit on Global Regulatory Issues

November 4, 2019

Outline

- The case for global regulatory convergence
- Timing for global education and harmonization
- Overcoming barriers to delivering gene therapy
- Practical next steps

Bottom Line Up Front

- Delivering safe and effective gene therapies to those in need should be a global priority to alleviate suffering from various serious diseases
- Global regulatory convergence in high income countries could help facilitate commercial availability and pave the way for the use of gene therapies in low and middle income countries

Approved Gene Therapies

- United States
  - Kymriah (2017)
  - Yescarta (2017)
  - Luxturna (2018)
  - Zolgensma (2019)
- European Union
  - Strimvelis (2016)
  - Kymriah (2018)
  - Yescarta (2018)
  - Luxturna (2018)
  - Zynteglo (2019)

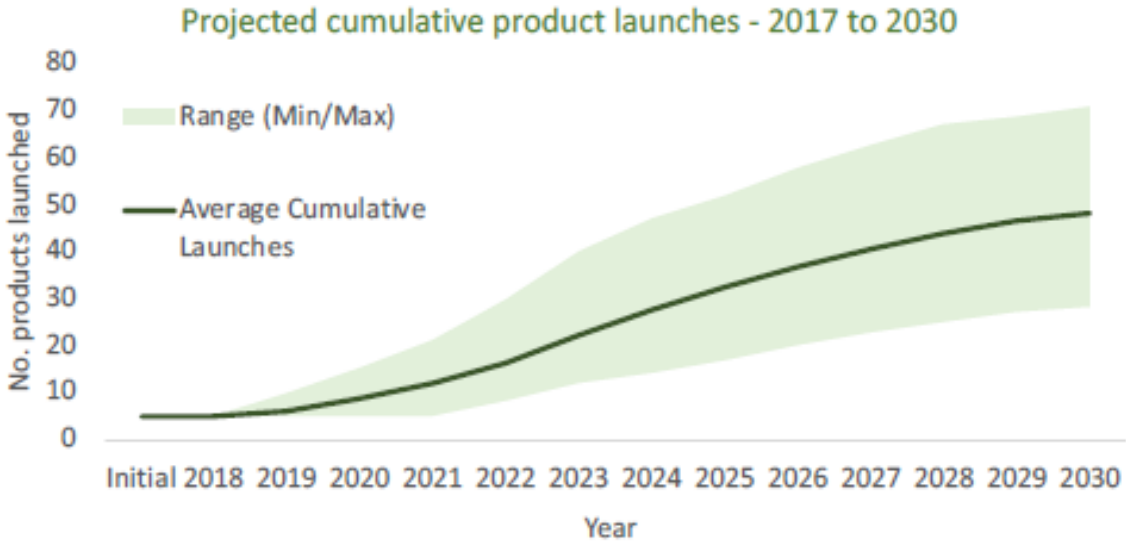
Glybera (approved 2012, withdrawn 2017)

Robust Global Pipeline

- Hemophilia A and B
- Retinal disorders
- Lysosomal storage disorders
- Neuromuscular diseases
- Hemoglobinopathies
- Cancers (genetically-modified T cells)

Gene Therapy Projections

Prediction of 40 to 60 product launches and more than 500,000 treated by 2030



From: MIT NEWDIGS Research Brief 2018F210-v027-Launches

Commercial Viability in 2019

Approximate Treatment Population Per Year

1-100 >100-10,000 >10,000

Importance of Gene Therapy for Rare Disorders

- There are hundreds of disorders affecting a few hundred individuals per year that could potentially be addressed by gene therapy
- Evolution of gene therapy toward increased use of genome editing may transform more common disorders into a collection of rare disorders

Global Regulatory Convergence: High Income Countries

- Robust commercial viability requires at least about 200 gene therapy treatments per year
- Any one country may not have enough patients to make many products commercially viable
- However, marketing across high income countries could result in commercial viability

Global Regulatory Convergence: Low and Middle Income Countries

- Populations in low and middle income countries may stand to benefit the most from gene therapy because of lack of access to supportive care
- Relying on a provided regulatory framework and on harmonized regulatory decisions equivalent to “pre-qualification” could help facilitate access

Regulatory Needs: Low and Middle Income Countries

- Many countries have little or no experience with the regulation of cell or gene therapies
- The availability of a globally-developed general regulatory framework could ultimately expedite patient access, since developing regulations out of nothing could be quite challenging

Manufacturing Needs: Low and Middle Income Countries

- Production of viral vectors in current generation of cell lines is relatively inefficient and costly
- Purification procedures for gene therapies are complex and are not standardized
- Concerted effort required to reduce cost of production and easy of therapeutic delivery

Importance of Global Collaboration for Gene Therapy

- Science of gene therapy is evolving rapidly and manufacturing technology is lagging behind
- The effect of a poorly conceived or improperly manufactured product on the entire field of gene therapy could be chilling, regardless of where the product is produced or administered

Potential Areas for Convergence

- Preclinical study requirements
  - Toxicology studies
- Environmental assessments
- Manufacturing information
  - Identity, purity, potency
- Clinical outcomes

Practical Next Steps

- More active harmonization of regulatory approach in high income countries
  - Meetings between US, EU, Canada, others
- Encourage sponsors considering global development programs that include the US to invite other regulators to early stage meetings (INTERACT, pre-IND)

Practical Next Steps

- Produce white paper on potential regulatory framework for cell and gene therapies for low and middle income countries
- International collaboration on advancing methods for production of gene therapies
- Develop public-private partnerships that can facilitate gene therapy for ultra rare disorders

Summary

- Delivering safe and effective gene therapies to those in need should be a global priority to alleviate suffering from various serious diseases
- Global regulatory convergence in high income countries could help facilitate commercial availability and pave the way for the use of gene therapies in low and middle income countries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