Session 056: Specialty Pharmacy Pipeline Update and Management Concepts for Gene Cell Therapies

SOA Antitrust Compliance Guidelines
SOA Presentation Disclaimer

2019 ANNUAL MEETING & EXHIBIT

Session 56: Specialty Pharmacy Pipeline Update and Management Concepts for Gene and Cell Therapies

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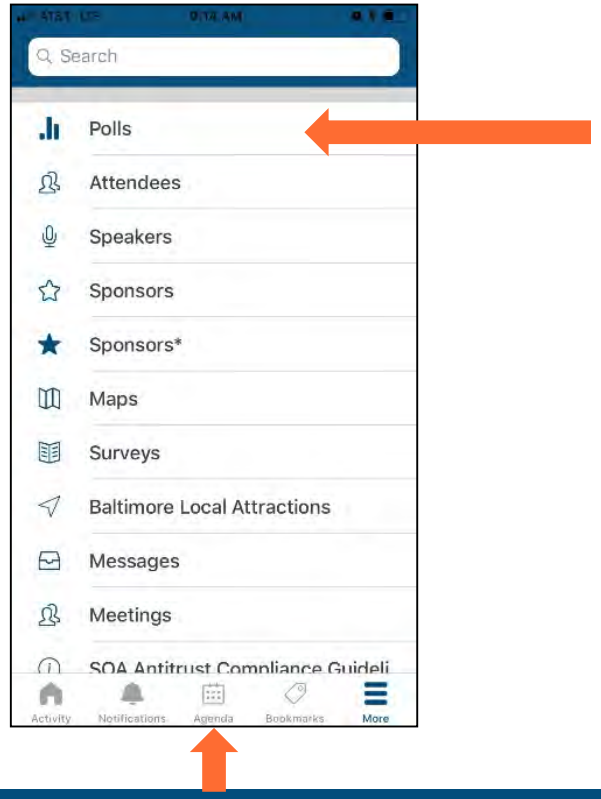

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Update on Biosimilar Uptake and Pipeline

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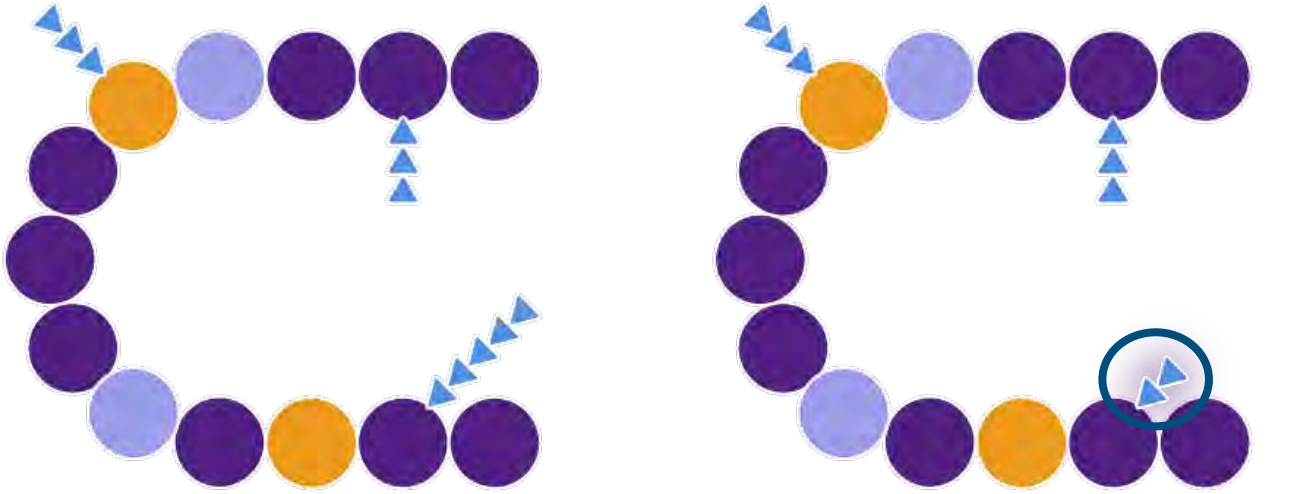
Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: How are biosimilars different from generics?

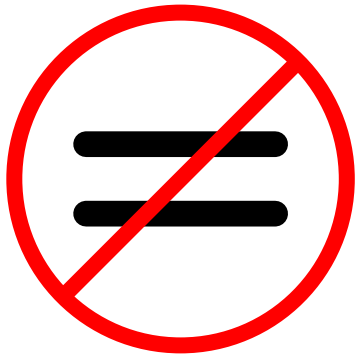
What are biosimilars?

- Highly similar (but not identical) to a *reference biologic*
  - Biologic: Large, complex drugs derived from a living organism
- No clinically meaningful difference in terms of safety, purity and potency



Reference medicine Biosimilar medicine

https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products

Biosimilar  Generic

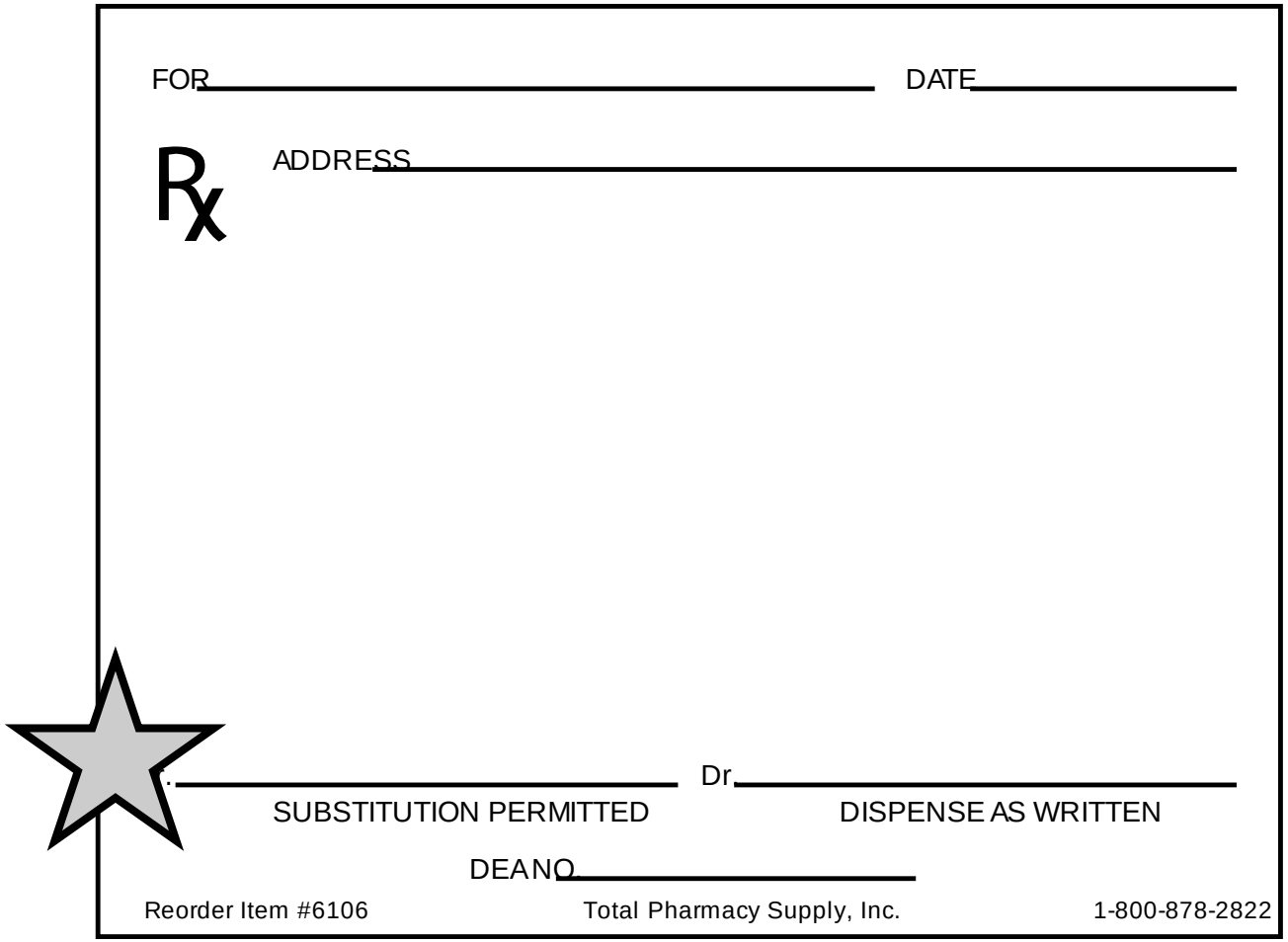
Biosimilars are not generics

- Biosimilars are *not interchangeable*
  - Slight variations between different batches of the same product, even those of reference products
- *Complex manufacturing* process
  - It takes years to bring a biosimilar to market
- Typically *large molecules*
- *Modest discounts (20-30%) relative to reference products*
  - Discounts expected to increase with multiple competing biosimilars
- Potential for $25 to $150 billions in savings in the next 10 years[1]
  - Generic savings of $1.7 trillion between 2004 and 2016 ($250 billion in 2016 alone)[2]

1 www.rand.org

2 www.accessiblemeds.org/resources/reports/2017-aam-annual-report

Automatic Generic Substitution



Biosimilars are not interchangeable

- Per the Hatch-Waxman Act of 1984, biosimilars approved under section 351(k) rely on safety and efficacy data from the reference product
- Biosimilar manufacturers must provide additional data showing that switching between the reference product and the biosimilar will have no effect on safety or efficacy
- Switching studies may be considered an unnecessary obstacle
  - A recent study from March 2018, comparing global data spanning over 20 years, shows that when patients switch from reference product to biosimilar, there were no meaningful differences in safety or efficacy
- Due to the nature of how biologics are produced, there are slight variations between different batches of the same product including reference products

Live Content Slide

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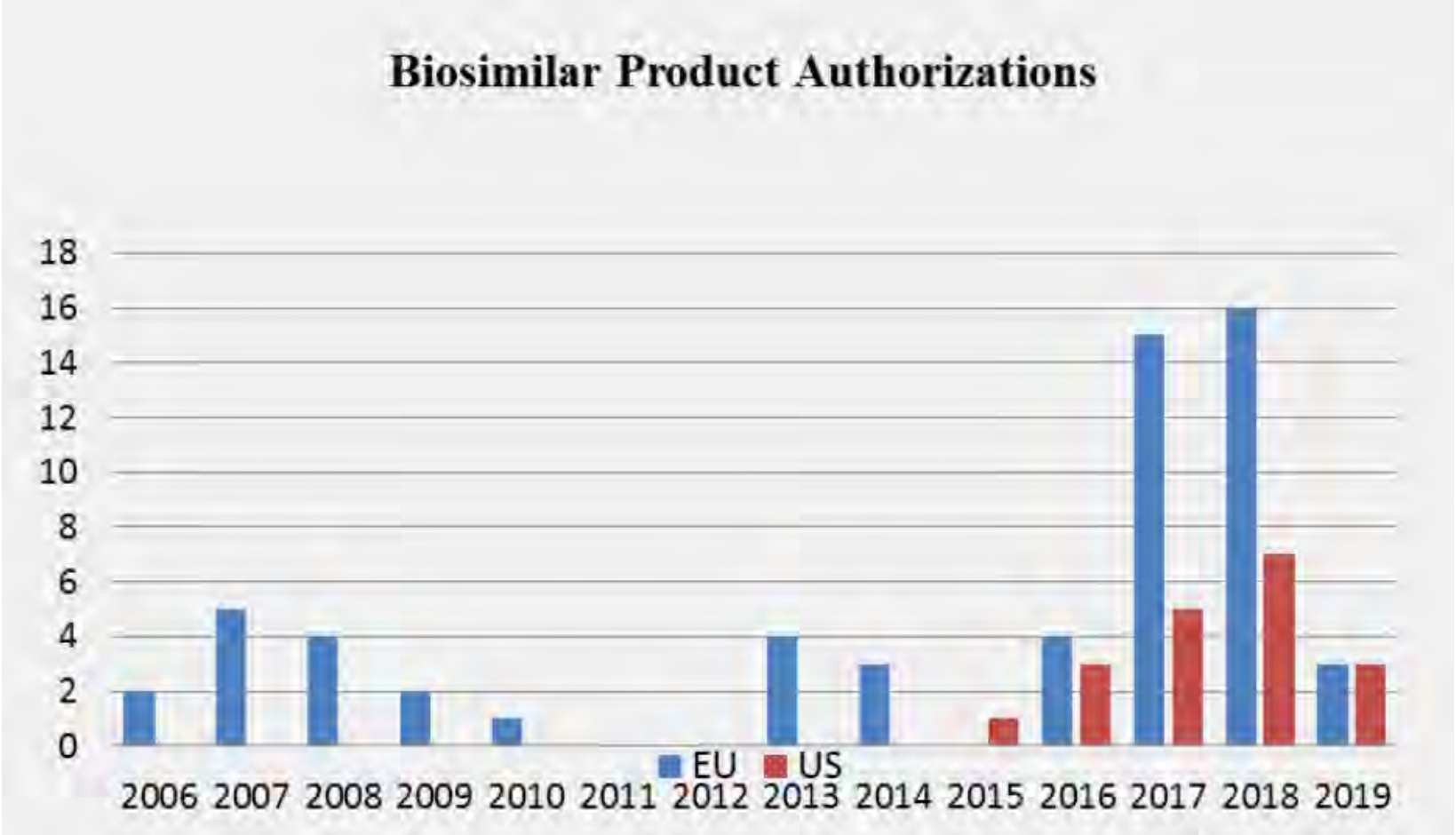
Poll: How many biosimilars have been approved in the US?

Biosimilar approvals in the U.S. lag behind Europe by almost a decade



https://www.biosimilarsip.com/2019/05/07/how-the-u-s-compares-to-europe-on-biosimilar-approvals-and-products-in-the-pipeline-4/

Biosimilar (and biosimilar-like) FDA approvals

Product	Class	Reference Product	Approval Date	Recipient
Herzuma; trastuzumab-pkrb	Her2 mAb	Herceptin	12/15/2018	Teva; Celltrion (manuf.)
Truxima - rituximab-abbs	CD20 mAb	Rituxan	11/28/2018	Celltrion
Udenyca; pegfilgrastim-cbqv	G-CSF, PEG-, rec. protein	Neulasta	11/2/2018	Coherus BioSciences; KBI Biopharma (manuf.)
Hyrimoz; adalimumab-adaz	TNF mAb	Humira	10/31/2018	Sandoz/Novartis
Nivestym; filgrastim-aafi	G-CSF, rec. protein	Neupogen	7/18/2018	Pfizer
Fulphila; pegfilgrastim-jmdb	G-CSF, PEG-, rec. protein	Neulasta	6/4/2018	Mylan GmbH
Retacrit; epoetin alfa-epbx	EPO, rec. protein	Epogen/Amgen and Procrit/J&J	5/17/2018	Hospira, Pfizer Inc
Ixifi; infliximab-qbtx	TNF mAb	Infliximab	12/13/2017	Hospira, Pfizer Inc
Admelog; insulin lispro*	Insulin analog	Humalog	12/5/2017	Sanofi
Ozempic; semaglutide*	GLP-1 analog	Victoza	12/5/2017	Novo Nordisk
Ogivri - trastuzumab-dkst	Her2 mAb	Herceptin	12/5/2017	Mylan and Biocon
Mvasi ; bevacizumab-awwb	VEGF mAb	Avastin	9/14/2017	Sanofi
Admelog; insulin lispro*	Insulin analog	Humalog	9/1/2017	Sanofi
Cyltezo; adalimumab-adbm	TNF mAb	Humira	8/25/2017	Boehringer Ingelheim
Lusduna Nexvue; insulin glargine*	Insulin analog	Lantus	7/24/2017	Merck & Co., Inc. (with Samsung)
Amjevita; adalimumab-atto	TNF mAb	Humira	9/23/2016	Amgen
Erelzi; etanercept	TNF mAb	Enbrel	8/26/2016	Sandoz/Novartis
Inflectra; infliximab-dyyb	Remicade	Remicade	4/5/2016	Janssen/Johnson & Johnson (Celltrion manuf.)
Basaglar; insulin glargine*	Insulin analog	Lantus	12/16/2015	Boehringer Ingelheim
Zarxio; Zarzio; filgrastim-sndz	G-CSF, rec. protein	Neupogen	3/6/2015	Sandoz/Novartis

* indicates 505(b)(2) NDA generic drug biosimilars-like approvals

Despite accelerating approvals, litigation and agreements between biologic manufacturers and biosimilar approval recipients are likely to delay their launch.

Source: https://www.biosimilardevelopment.com/doc/biosimilars-pipeline-shows-remarkable-sustained-growth-0001

Live Content Slide

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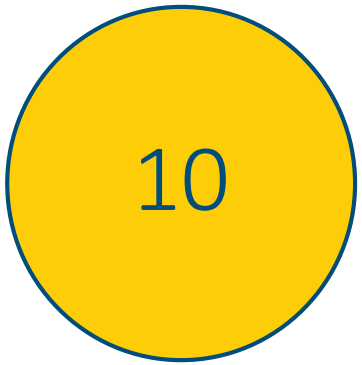
Poll: How many biosimilars have been launched in the US?

Comparison of U.S. Approvals vs. Launch

U.S. Biosimilar Launches as of August 2019

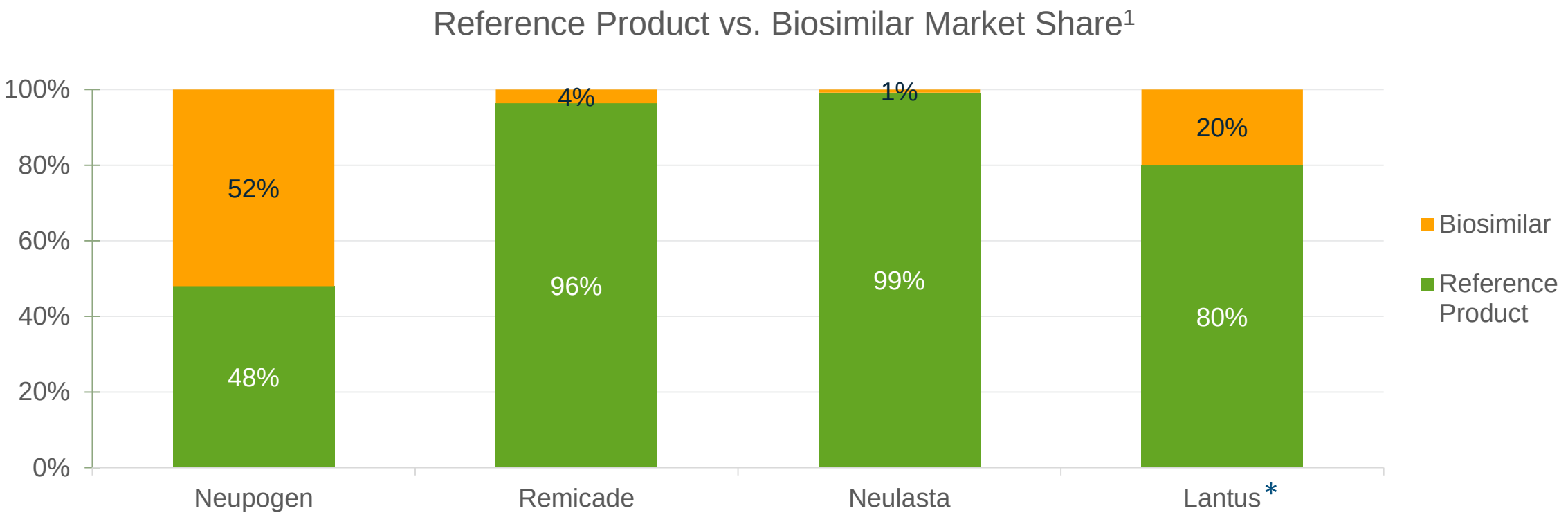


U.S. Approvals 2015 – 2018

Biosimilar	Reference Drug	Approval Date	Launch Date
Zarxio	Neupogen | Granix	3/6/2015	Sep-15
Inflectra	Remicade	4/5/2016	Nov-16
Erelzi	Enbrel	8/30/2016	
Amjevita	Humira	9/23/2016	2023
Renflexis	Remicade	4/21/2017	Jul-19
Cyltezo	Humira	8/25/2017	2023
Mvasi	Avastin	9/14/2017	Jul-19
Ogivri	Herceptin	12/1/2017	2019?
Ixifi	Remicade	12/13/2017	N/A*
Retacrit	Epogen | Procrit	5/15/2018	Jun-19
Fulphila	Neulasta	6/4/2018	Jul-19
Nivestym	Neupogen | Granix	7/20/2018	Mar-19
Hyrimoz	Humira	10/30/2018	2023
Udenyca	Neulasta	11/2/2018	Nov-19
Herzuma	Herceptin	12/14/2018	2019?

*Will not be launched in the US

Overall Biosimilar Utilization in U.S.[1]



* Comparison is against the 100 Unit/mL formulation only. Currently insulins are not-considered biologics and biosimilars, but will make that transition in 2020.

Sources: 1. MedImpact: 2018-2019 Pharmaceutical Marketplace Trends. Available at: https://conference.medimpact.com/documents/398252/453336/MedImpact+2019+0415.pdf/e440e7d0-8e65-4bc4-90c0-457ef25cf004. Published April 15, 2019. Accessed September 10, 2019.

Pipeline: biologics with expired or near expiring patents in the U.S.

Biosimilars for at least 23 different original biologics are currently navigating biosimilar pathways or are in late stage development in the U.S.

Drug Product	Primary U.S. Patent Expiry
OnabotulinumtoxinA (Botox®)	Primary patents long-expired, various use patents pending
Filgrastim (Neupogen®)	2013
Epoetin alfa (Epogen®)	2013
Pegfilgrastim (Neulasta®)	2015
Adalimumab (Humira®)	2016
Rituximab (Rituxan®)	2018
Cetuximab (Erbitux®)	2018
Omalizumab (Xolair®)	2018
Infliximab (Remicade®)	2018
Bevacizumab (Avastin®)	2019
Trastuzumab (Herceptin®)	2019
Tocilizumab (Acetmra®)	2019
Abatacept (Orencia®)	2019
Ranibizumab (Lucentis®)	2020
Eculizumab (Soliris®)	2021
Aflibercept (Eylea®)	2023
Denosumab (Prolia® and Xgeva®)	2023
Ustekinumab (Stellara®)	2023
Certolizumab pegol (Cimzia®)	2024
Golimumab (Simponi®)	2024
Darbepoetin alfa (Aranesp®)	2024
Ipilimumab (Yervoy®)	2025
Etanercept (Enbrel®)	2028

Source:

https://www.biosimilarsip.com/2019/05/07/how-the-u-s-compares-to-europe-on-biosimilar-approvals-and-products-in-the-pipeline-4/

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Emerging Gene & Cellular Therapies

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Rare Diseases / Orphan Drugs

- Rare Diseases[1]
  - A condition affecting ≤ 200,000 people in the [United States]
  - A condition affecting less than 1 in 2,000 [European Union]
  - Approximately 7,000 rare diseases impacting ~25-30M Americans
  - "In the United States, only a few types of rare diseases are tracked when a person is diagnosed. These include certain infectious diseases, birth defects, and cancers. It also includes the diseases on state newborn screening tests. Because most rare diseases are not tracked, it is hard to determine the exact number of rare diseases or how many people are affected."
- Orphan Drug Act (1983)
  - Passed to encourage the development of drugs for rare disorders
  - Created the prevalence definition (above), in situations where, "there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from the sale in the United States."[2]

[1] https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases
[2] Health Promotion and Disease Prevention Amendments of 1984, Pub. L. 98–551, 98 Stat 2815 (1984)

Gene & Cell Therapies are Making Headlines

HEALTHCARE NOVEMBER 5, 2018 / 8:39 AM / 6 MONTHS AGO

Novartis says SMA gene therapy is cost-effective at $4-5 mln per patient

Reuter's Healthcare, 11/5/2018

Cigna aims to expand affordable access to gene therapies

SHELBY LIVINGSTON, Modern Healthcare, 9/6/2019

New gene editing technology could correct 89% of genetic defects

By Jessie Yeung, CNN, 10/22/2019

Scientists Designed a Drug for Just One Patient. Her Name Is Mila.

NY Times, Gina Kolata, October 9,20189

Gene Modifying Therapy vs. CAR T[1]

Gene Therapy

- Gene Therapy involves the transferring of genetic material into a patient.
- The genetic material changes how protein(s) is/are produced by targeted cells.
- The result is the introduction, removal, or change in the content of a person's genetic code to treat or cure the disease.
- Carriers/vectors transport the genetic material to the targeted cells.

Cell Therapy

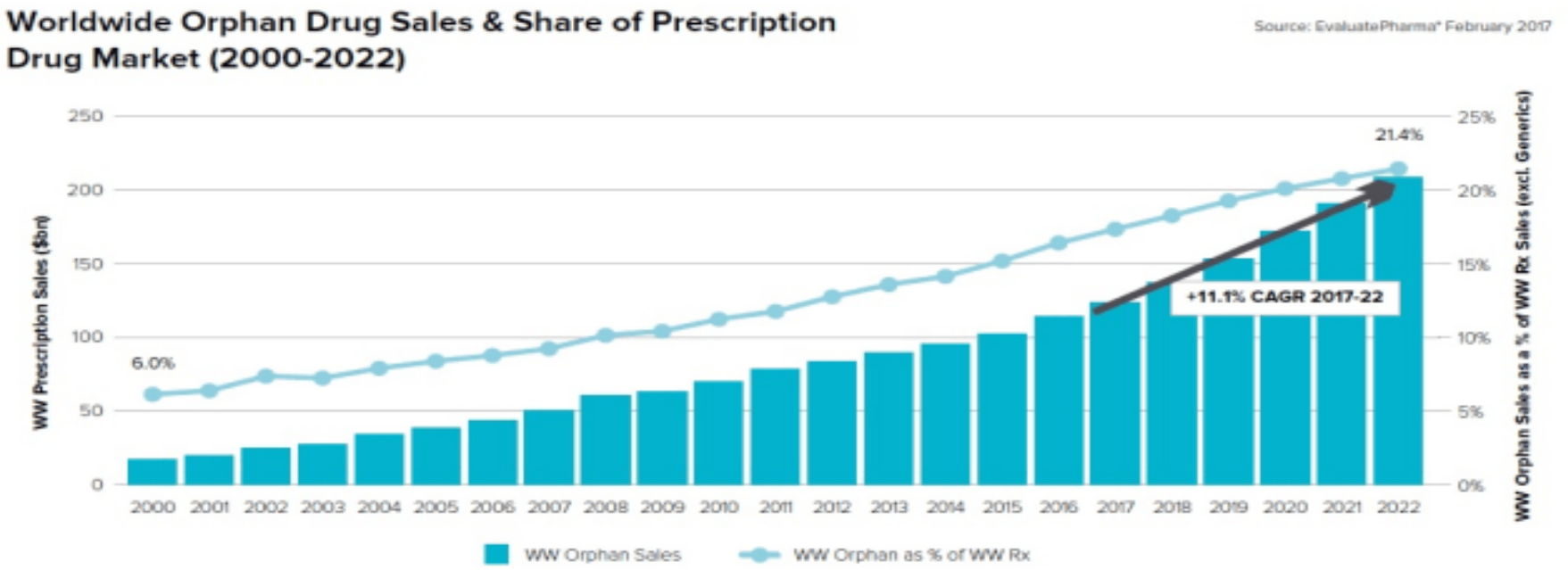
- Cell therapy is the transfer of intact, live cells into a patient to help lessen or cure a disease. The cells may originate from the patient (autologous cells) or a donor (allogeneic cells).
- The type of cells administered depends on the treatment (e.g., pluripotent, multipotent, and primary).
- Chimeric Antigen Receptor (CAR) T-cell therapy modifies a patient's own immune cells (T-cells), which attach to antigens on the surface of cancer cells.

[1] https://www.asgct.org/education/more-resources/gene-and-cell-therapy-faqs (accessed May 7, 2019)

Currently Marketed Gene / Cell Products

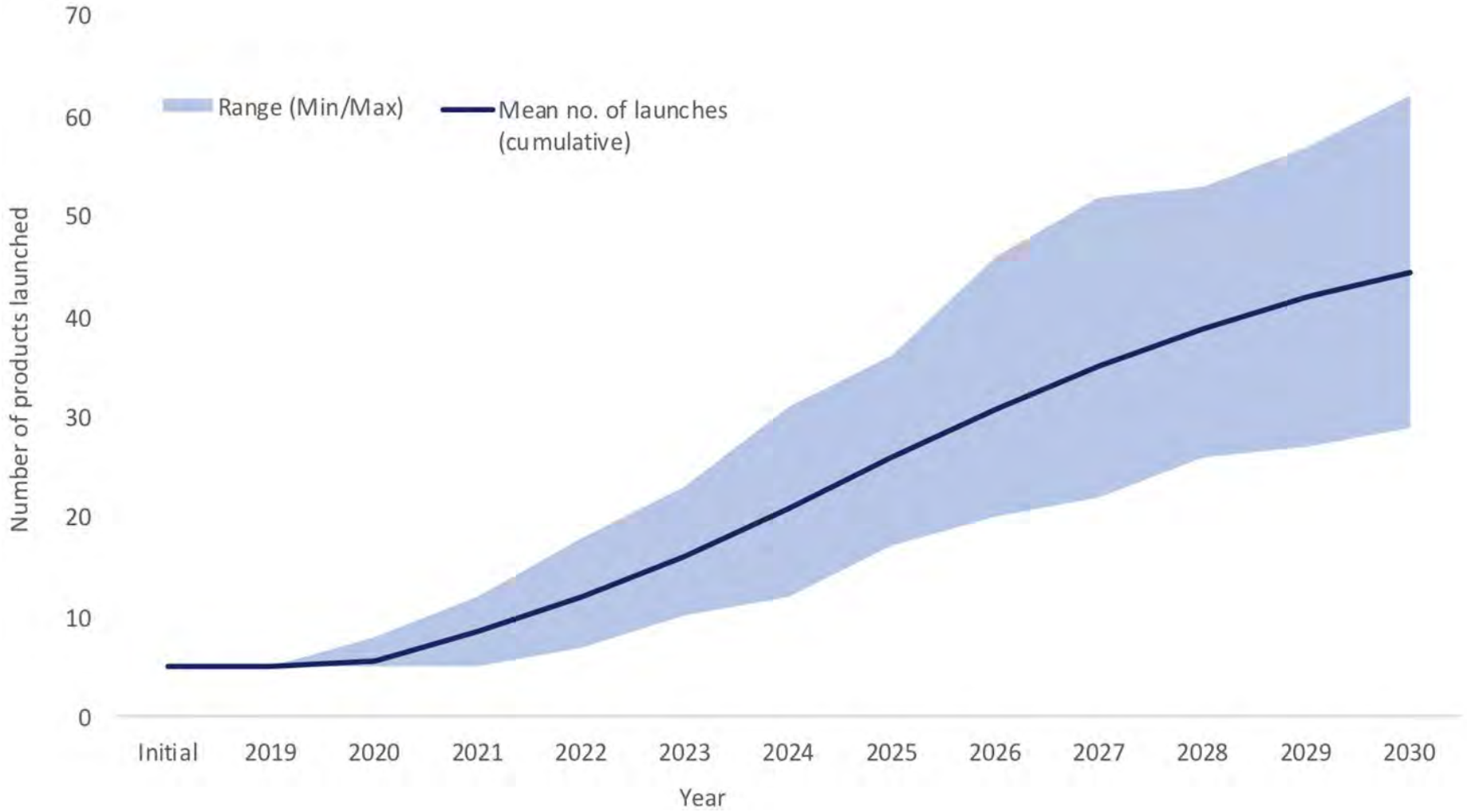
Therapy	Company	Approval Date	Therapy Type	Indication	Treatment Cost
Provenge	Dendreon Pharmaceuticals	April-2010	CAR T	Asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer	$63,000 per dose
Imlygic	Amgen	October-2015	Viral	Local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery	$150,000 annually ($6,000 every 2 weeks)
Kymriah	Novartis	August-2017	CAR T	Specific instances of B cell acute lymphoblastic leukemia	$570,000
Yescarta	Kite/Gilead	October-2017	CAR T	Relapsed or refractory large B-cell lymphoma	$450,000
Luxterna	Spark Therapeutics	December-2017	Gene	Leber congenital amaurosis or retinitis pigmentosa	$500,000 (per eye)
Zolgensma	Novartis	May-2019	Gene	Type 1 Spinal Muscular Atrophy	$2.1M

Robust Pipeline of Orphan Therapies



- Worldwide orphan drug sales are forecast to total $209 billion and growing at a rate of **11.1%** from 2017 to 2022, more than twice the rate predicted for conventional drugs
- The market for orphan drugs is anticipated to be **21.4%** of worldwide prescription sales by 2022 (excluding generics)
- The worldwide pipeline includes over 1,100 therapies targeting over 60 rare conditions

Potential Launch Trajectory



Source: Estimating the Clinical Pipeline of Cell and Gene Therapies and Their Potential Economic Impact on the US Healthcare System. Casey Quinn, PhD,* Colin Young, PhD, Jonathan Thomas, BSc, Mark Trusheim, MSc, and the MIT NEWDIGS FoCUSWriting Group VALUE HEALTH. 2019; 22(6):621–626.

Why Payers Should Care

- Gene Therapies carry significant actuarial risk
  - Unknown and potentially volatile number of affected patients
  - Anticipated costs per treatment in the range of $500K to $5M
  - Durability, or endurance, of these new therapies is typically unknown.
  - Treatment costs are all front-loaded, rather than over time for traditional medicine/therapies/claim costs
  - Benefit design and adverse selection
  - Type and time horizon of value will vary dramatically from disease state to disease state
  - Patient migration
  - FDA hiring additional reviewers to expedite review of anticipated INDs
- Internal inefficiencies in developing management plans for a small number of potential patients
- External inefficiencies in establishing treatment networks and contracting with manufacturers

Source: Improving Management of Gene and Cell Therapies: The Orphan Reinsurer and Benefit Manager (ORBM). Trusheim, M et. al. Pharmaceutical Executive, September 10, 2018

Recent Orphan Drug Strategy Project

The goal

Assess current membership and claims experience to forecast the cost of gene therapies over the next 3-5 years.

Claims Analytics

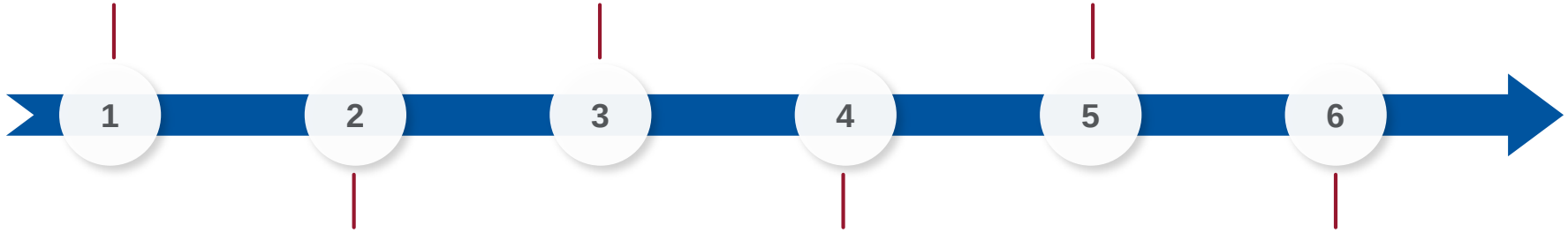
Research gene tx pipeline and related ICD-10 codes

Clinical Research

Clinical assessment of current rare disease treatment options & costs

Modeling & Planning

Developed actuarial model to forecast growth in treatment costs and anticipated cost offsets

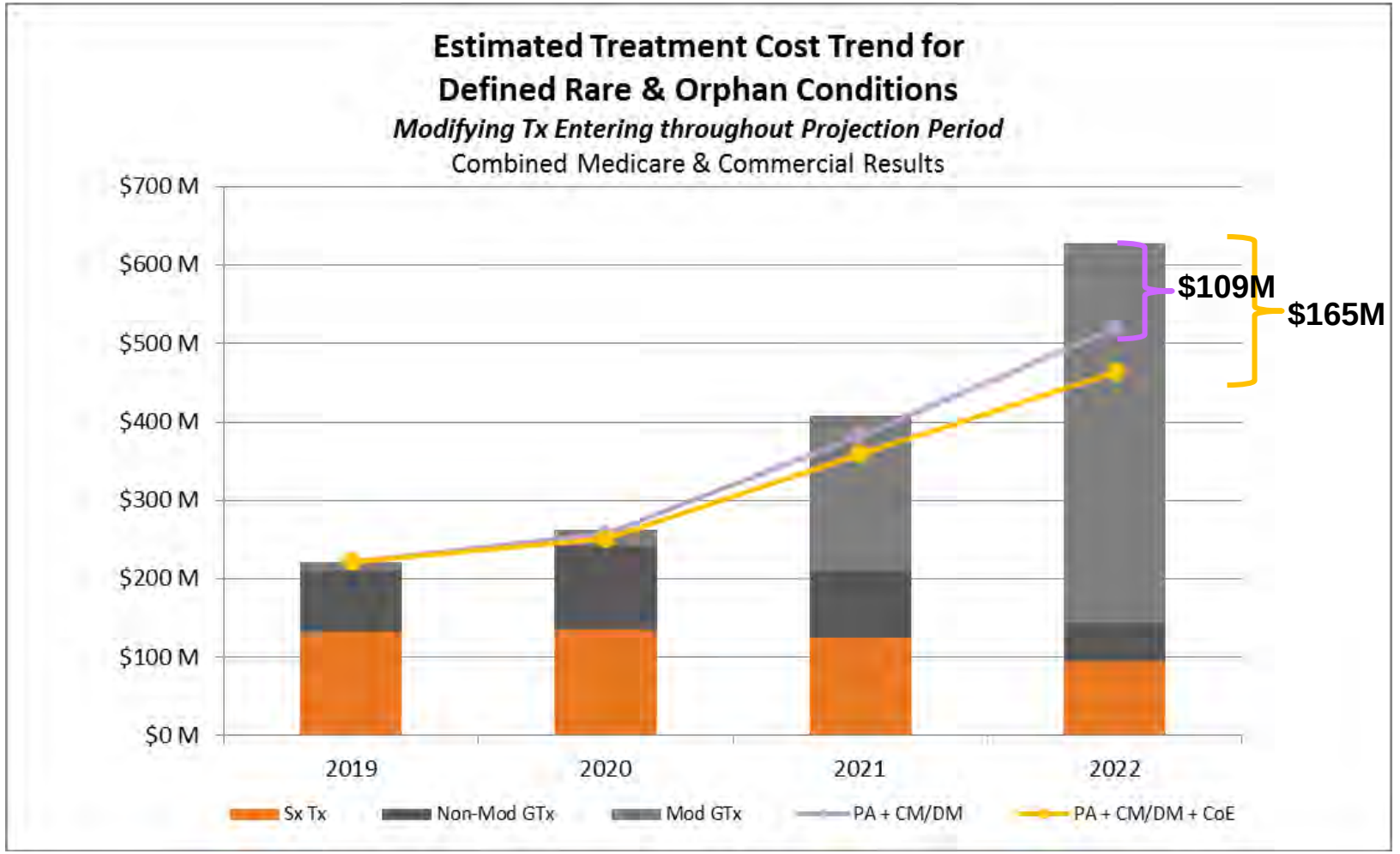


2. Analyze claims experience to quantify rare disease membership exposure and associated treatment costs

4. Clinical assessment of pipeline gene therapies (e.g., subpopulations, place in therapy)

6. Build a planning framework to prepare cost, benefit, and clinical management in advance of gene therapies

Recent Orphan Drug Strategy Project (Cont'd)



- ***Medicare*** includes estimates for the following disease states: Scleroderma, Amyotrophic lateral sclerosis (ALS), Huntington's disease, Alpha-1 antitrypsin deficiency, sickle cell Anaemia, and Spinal muscular atrophy
- ***Commercial*** includes estimates for the following disease states: Cystic fibrosis, sickle cell Anaemia, Hemophilia A & B, Amyotrophic lateral sclerosis, Aromatic L-amino acid decarboxylase (AADC) deficiency, and Spinal Muscular Atrophy

Orphan Reinsurer & Benefit Manager Concept

- Creating financing solutions for durable/potentially curative therapies with large, upfront costs whose benefits accrue over time

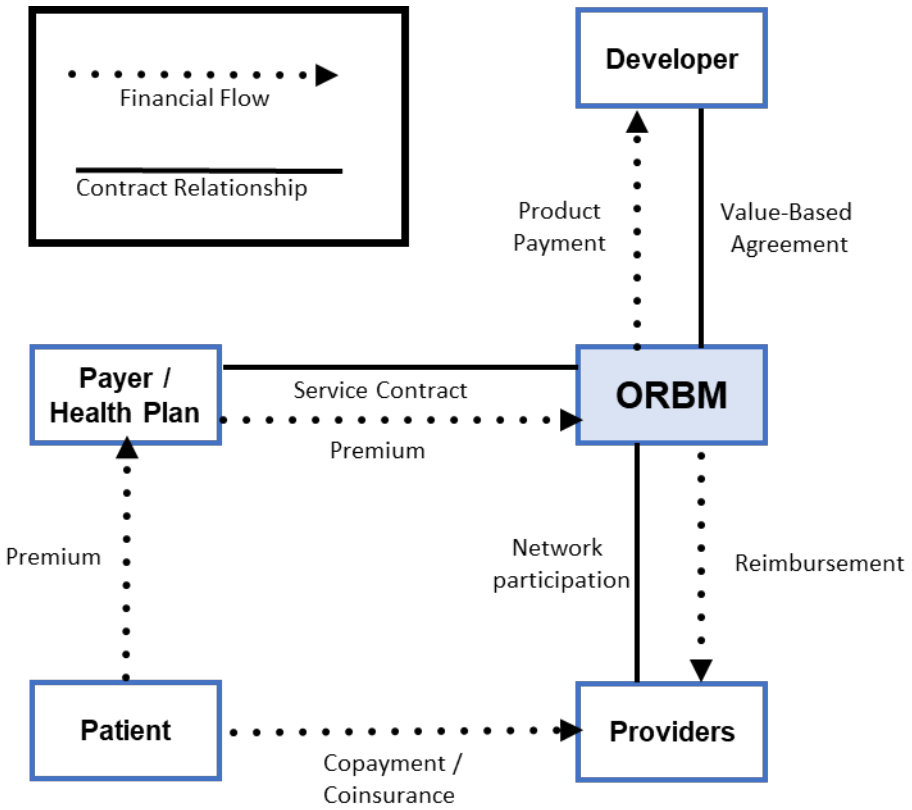
Financial Challenges

- Timing of claim payments
- Actuarial risk
- Therapeutic outcomes risk (e.g,. durability, efficacy)

Key Features

- Consolidate risk—carve-out and pool risk
- Contracting and payment
- Care coordination services
- May be National or Regional in scope

Orphan Reinsurer and Benefit Manager (ORBM) interactions



Source:
Trusheim M, Mytelka DS, Warren GL, Han D, Ciarametaro M. Improving Management of Gene and Cell Therapies: The Orphan Reinsurer and Benefit Manager (ORBM). PharmExec 2018 Sept 10. Available at: http://www.pharmexec.com/improving-management-gene-and-cell-therapies

Outcomes-Based Risk-Sharing Agreements (OBRSA)

- Potential payer benefits:
  - Optimized resource utilization and patient outcomes
  - Competitive product offerings
  - Member retention and growth
  - Financial sustainability
  - Positive public relations
  - Move away from a rebate-based reimbursement model
- Potential manufacturer benefits:
  - Maintained or improved formulary access
  - Competitive differentiation and growth
  - Financial sustainability
  - Generation of real-world evidence of value
  - Move away from a rebate-based reimbursement model

Source: Warren GL, Ou W, Gregor K. Partnering to Share the Risk. The Actuary Dec 2018/Jan 2019, Vol 15, Issue 6. Available at: https://theactuarymagazine.org/issue/december-2018-january-2019/

Cigna/Express Scripts Roll-out Early Offering

Source: Cigna Corp, accessible at https://www.multivu.com/players/English/8600151-cigna-express-scripts-embarc-benefit-protection/

- Key concepts†:
  - Targets health plans, employers and union trust funds
  - 'Anticipated' fee of < $1.00PMPM, still to be finalized
  - Unclear what 'best possible price tag' for plan sponsors means relative to 'predictable plan costs'
  - Currently applies to the two marketed gene therapies
  - Prior authorization process determines patient eligibility
  - No cost share to patients/members
  - Embarc℠ manages payment for the cost of therapies
  - Open to additional therapies (e.g., Car-T)
  - Appears to be open to competitors

† https://www.modernhealthcare.com/payment/cigna-aims-expand-affordable-access-gene-therapies. Accessed October 22, 2019.

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Case Study—Outcomes-Based Risk Share Arrangements

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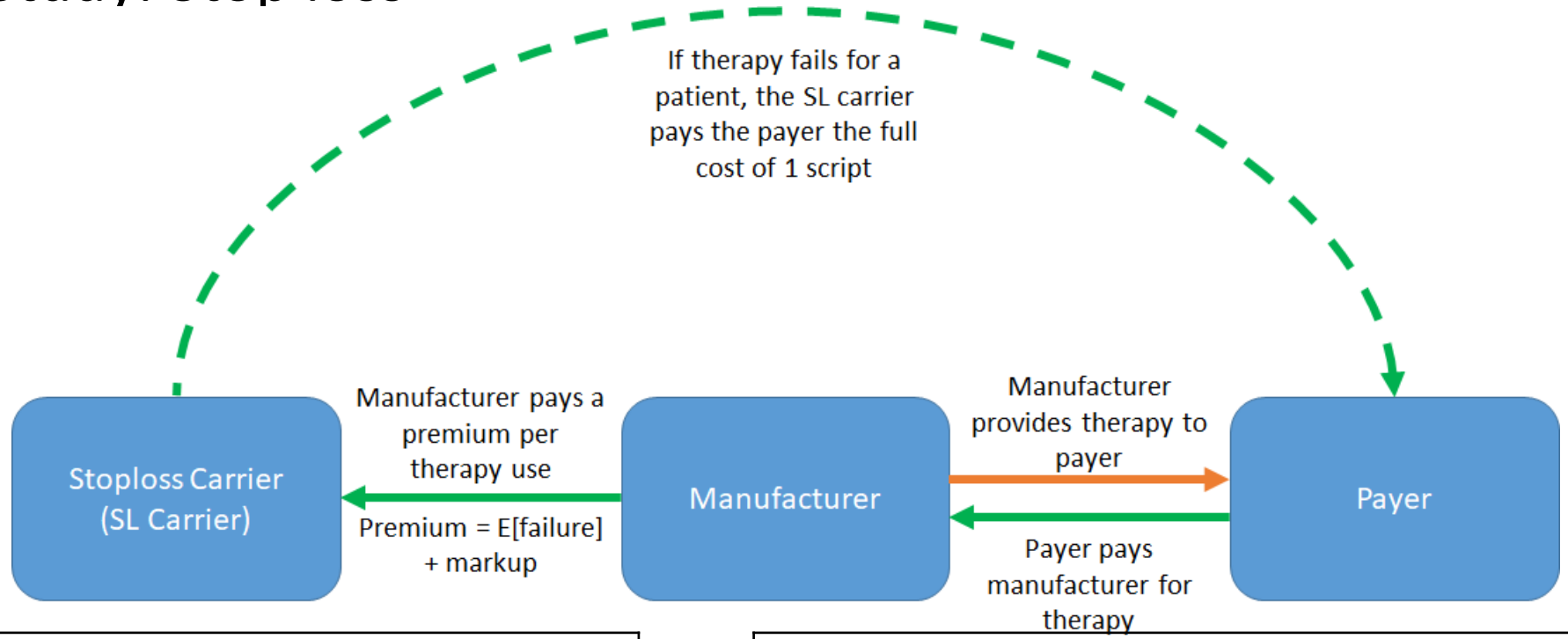
Considerations for outcomes-based contracting for gene & cell therapies

- Manufacturer
  - Risk
  - Anti-Kickback Statute
  - Medicaid best price rule
- Government (CMS)
  - CMS is encouraging value-based contracting
  - Could waive Medicaid best price and anti-kickback barriers
- Payer
  - Possibility of patient ‘clustering’ (genetic disorders may appear in siblings)
  - Reinsurance ‘lasering’

Outcomes-based contracting

Case Study: Stop loss



Assumptions	
Therapy Cost (per Patient)	$1,000,000
Expected failure rate	10%
Number of patients treated	20
Expected (and actual) number of failures	2
MLR Stop Loss	60%

Flow of Funds under Stop Loss Agreement

	Manufacturer	Stop Loss Carrier	Payer
Premium paid for stoploss	($3,333,333)	$3,333,333.33	$0
Initial payment for therapy	$20,000,000	$0	($20,000,000)
Refunds for therapy failures	$0	($2,000,000)	$2,000,000
Total	**$16,666,667**	**$1,333,333**	**($18,000,000)**