



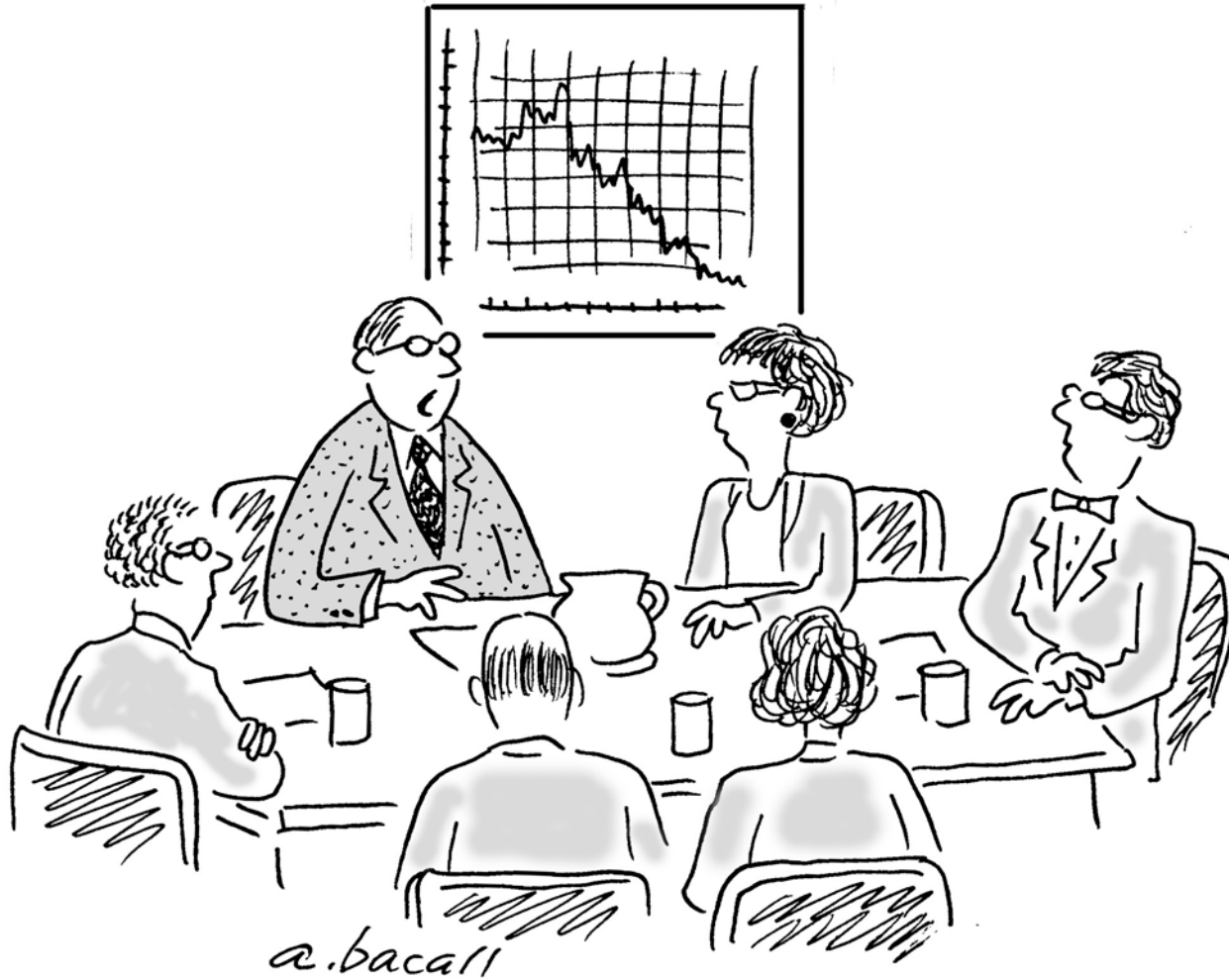
Cost, equity and access

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"Turning our dismal performance around might be easier if we eliminated our ethics committee."

Overview

- ▶ History
- ▶ Cost and recently approved gene-targeted therapies
- ▶ Innovation, cost and access
- ▶ Lessons from Spinal Muscular Atrophy
- ▶ The future: how can we proactively identify challenges and address them across the field?

Historical context

- ▶ Expensive drugs not being covered by insurance

Cost Savings

Between 2000 and 2005, annual critical care medicine costs increased from \$56.6 billion to \$81.7 billion, representing 13.4% of hospital costs, 4.1% of national health expenditures, and 0.66% of gross domestic product. Cost savings of up to \$1 billion per quality life year gained can be attained with critical care management of severe sepsis, acute respiratory failure, and general critical care interventions. Twenty-four-hour intensivist staffing reduces intensive care unit (ICU) costs and lengths of stay (LOS). Up to \$13 million in annual hospital cost savings can be realized when care is delivered by an intensivist-directed multiprofessional team. The impact of this type of care is demonstrated by the example of a community hospital that achieved 105% return on investment by implementing mandatory intensivist consultation and admission standards, thereby reducing ICU lengths of stay, ventilator-associated events, and central venous access device infection rates. Hospitals without on-site intensivists may benefit from telemedicine ICU, in which sophisticated electronic systems connect ICU patient data to intensivists at remote locations. The intensivists provide real-time monitoring, diagnostic, and intervention services in conjunction with bedside staff. In selected settings, tele-ICU (or e-ICU) care has demonstrated shorter ICU lengths of stay and lower ICU mortality, which may translate into lower hospital costs and better use of resources.

<https://www.sccm.org/Communications/Critical-Care-Statistics>

Glybera and LLD

- ▶ Approved in Europe in 2012 for treatment of lipoprotein lipase deficiency
- ▶ Long approval trajectory: developed in 2003, first human trial in 2005, second trial in 2007, 3rd in 2009, but did not meet major endpoint of reduction in episodes of pancreatitis requiring hospitalization
- ▶ Application for approval in 2009, met with concerns about long-term efficacy
- ▶ When approved: required postmarketing pharmacovigilance plan, biannual safety reports, registry and long-term follow up of patients
- ▶ “million dollar drug”; 60 people dosed in Europe, one paid for
- ▶ drug withdrawn in US, renewal not pursued in Europe



Spinraza and SMA

- ▶ Approved in the US in December 2016
- ▶ Antisense oligonucleotide that moderates splicing of the SMN2 gene, functionally converting it into the SMN1 gene, administered intrathecally
- ▶ Partial work funded by Cure SMA; Ionis and Biogen
- ▶ \$750,000 in first year, \$350,000 annually after that
- ▶ Insurance coverage variable, company covering some
- ▶ Approved in Canada, Japan, Brazil, Switzerland
- ▶ Denmark: only SMAI, Norway first rejected, then approved for <18
- ▶ UK and Ireland rejected because of cost
- ▶ In US: limited/variable coverage for SMA Types II, III and IV and for lack of response



Zolgensma and SMA



- ▶ AAV delivery of normal SMN1 gene, one time IV administration in babies; testing intrathecal injection for older kids and Types II-IV
- ▶ Cure SMA support, Avexis and Novartis
- ▶ Approval expected in Spring 2019
- ▶ Predicted costs: \$4-5 million
- ▶ Competition: Risdiplam (Roche) in pipeline, orally available small molecule taken for life
- ▶ Cost, convenience, effectiveness, compliance, side effects, access

Future cost challenges

- ▶ More common diseases on the near-term horizon (hemophilia, sickle cell, macular degeneration)
- ▶ FDA expects to approve 10-25 new gene therapies a year by 2025
- ▶ We won't be able to say it's just a few patients or a few diseases, even in the short term

Not your parents' expensive drug...

TREATMENTS

Drug Puts A \$750,000 'Price Tag On Life'

August 1, 2017 · 1:05 PM ET

JULIE APPLEBY

FROM **KHN**



Drugs that cost as much as a house are on the way to treat rare and devastating diseases. The US is scrambling to figure out how to pay for them.

Emma Court Mar. 4, 2019, 8:57 AM



Societal Concerns About Costs

EPIPEN PRICE UNDER MYLAN



SOURCE: Truven Health Analytics

TREATMENTS

As Drug Costs Soar, People Delay Or Skip Cancer Treatments

March 15, 2017 · 5:00 AM ET

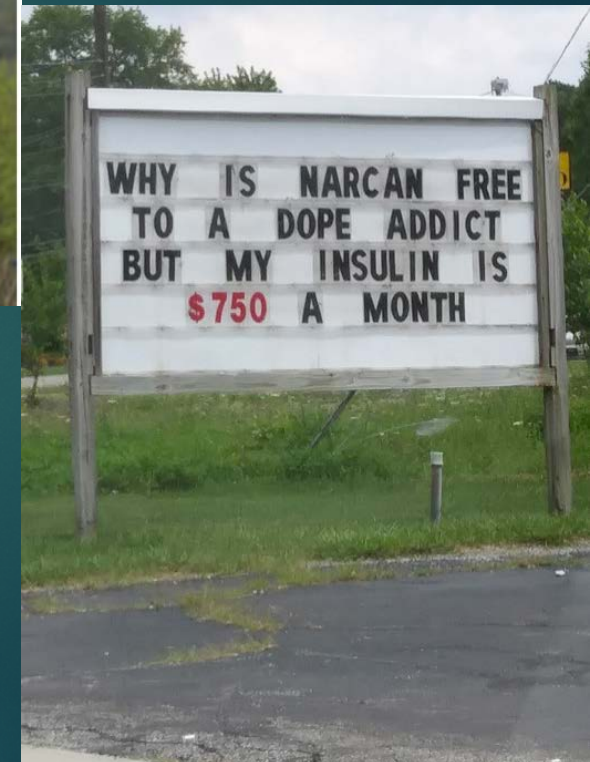
LIZ SZABO

FROM KHN



Friday, August 26, 2016
AAEC Ref Num: 153703

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Institute for Clinical and Economic Research (ICER)

- ▶ “The Institute for Clinical and Economic Review ([ICER](#)) is an independent non-profit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER’s reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.”

(ICER website)

- ▶ “ICER is attempting to boldly go where no US health technology assessment group has gone before, to engage the public in a discourse on healthcare value by presenting transparent and scientifically rigorous information on the clinical features of treatments, as well as on their long-term benefits to the patient, including the incremental costs to achieve those benefits, and the short-term economic impact on the healthcare system.”

(Pizzi, Am Health Drug Benefits, 2016)

Critiques of ICER

Critics target institute that evaluates price, value of drugs

Fernanda Crescente and Jayne O'Donnell, USA TODAY

Published 2:24 p.m. ET July 28, 2016 | Updated 3:13 p.m. ET July 28, 2016



Ad

Doctor
Nurse Social worker
Van driver
Dietitian
Home care aide

Senior care that lets you live in your home.

#Lifeways On Lok Lifeways

USA TODAY speaks with Founder and President of the Institute for Clinical and Economic Review, Dr. Steven Pearson about what tools ICER provides to customers. USA TODAY

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CVS
FiercePharma

MANUFACTURING MARKETING PHARMA VACC

Pharma

Patient groups rebuke CVS on ICER, saying cost-effectiveness reviews discriminate

by Eric Sagonowsky | Sep 14, 2018 12:00pm



Donna Cryer, founder of the Global Liver Institute, poses with her car and LIVRLADY license plate. A critic of ICER, she had a liver transplant 21 years ago due to an autoimmune condition. (Photo: Handout)

Value-Based Pricing for Emerging Gene Therapies: The Economic Case for a Higher Cost-Effectiveness Threshold

Louis P. Garrison, PhD; Tristen Jackson, PharmD, MS;
Douglas Paul, PharmD, PhD; and Mike Kenston, BS, MBA

SUMMARY

While one-time gene replacement therapies may offer transformative innovation for the management of ultrarare, health-catastrophic diseases, they also pose challenges to the current U.S. health care system. Historically, the United States and other countries have demonstrated a willingness to support higher prices for health gains in rare diseases. However, payers may be ill-prepared to address reimbursement based on single administrations associated with gene therapies. As yet, there is no consensus on how to

The development of one-time gene replacement therapies for ultrarare, health-catastrophic diseases heralds a new era of transformative innovation that may offer cures (or near cures) while reducing the high lifetime cost of medicines administered chronically. The United States and other countries have adopted regulations and incentives to encourage the development of orphan products for rare diseases and have, in practice, demonstrated some willingness to pay higher prices

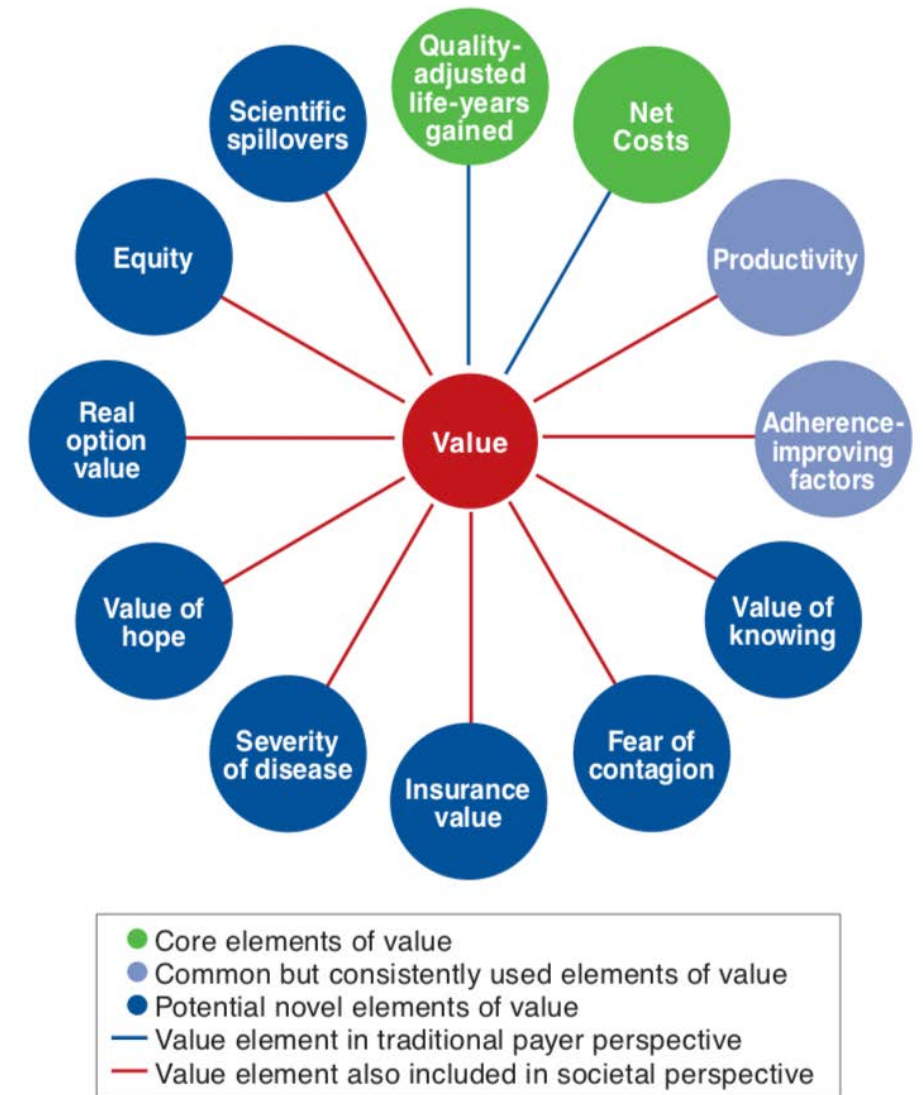
“These additional elements, we would argue, provide an economic rationale for defining a higher CET for proven life-saving therapies for ultrarare, health-catastrophic conditions...(2017).”

“The STF report also cites “severity of disease” as an element to consider. Since the utility scale (0 to 1) as reflected in the QALY assumes that a gain from 0.6 to 0.8 is equivalent to a gain from 0.2 to 0.4, it does not adjust for the latter, greater baseline severity of disease. Qualitative survey research in general populations suggests not all QALY gains are considered equal: people would generally give priority to subpopulations with poor baseline health, including those at end of life.”

Lakdawalla et al. Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3]. *Value Health*. 2018;21(2):131-39.

Garrison et al. Value based pricing for emerging gene therapies. The economic case for higher cost-effectiveness thresholds. *J Managed Care Specialty*. 2019. Published online.

FIGURE 1 Potential Elements of Value



Adapted from Lakdawalla DN, Doshi JA, Garrison LP Jr, Phelps CE, Basu A, Danzon PM. Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3].³⁶

Public-Facing Pushback

What's the value of your life to CVS?

CVS would like to exclude drugs from their formulary that don't meet a certain "value" threshold. This threshold is based on QALYs, which undervalue the lives of the disabled and chronically ill.



**When CVS
uses cost
thresholds,
patients
are left out.**



<http://www.pipcpatients.org/cvs.html>

QALY (Quality Adjusted Life Year) vs. evLYG (Equal Value of Life Years Gained)

- ▶ “with growing use of ICER reports to inform drug price negotiations and insurer coverage, concerns have been raised that the use of the QALY could undervalue treatments that extend length of life without improving quality of life. To address this concern of discrimination directly, and ensure that all stakeholders can engage with cost-effectiveness in confidence that it provides analyses that value a year of life for all patients exactly the same, **ICER’s future reports will prominently feature a calculation of the Equal Value of Life Years Gained (evLYG)**. The evLYG is not as flexible as the QALY in capturing benefits to quality of life but does measure any gains in length of life exactly the same across all conditions, regardless of age, severity of illness, or level of disability.”
- ▶ “By highlighting the evLYG measure of health gain, we are responding to deeply held feelings expressed by some critics that the QALY could discriminate against vulnerable patient groups. We hope that raising the profile of the evLYG will reassure them and policymakers that when treatments offer the opportunity to extend lives, between the QALY and the evLYG we will make sure that each day, month, or year of extra life will be valued equally.”

Steven Pearson, President ICER, December 12, 2018

<https://icer-review.org/announcements/icer-describes-qaly/>

ICER: Spinraza vs. Zolgensma

- ▶ “Both of these treatments appear to dramatically improve the lives of children with SMA, as well as the families who take care of them,” said David Rind, MD, ICER’s Chief Medical Officer. “And while Spinraza has a broader body of evidence that provides more certainty around the health benefits patients may receive, the limited data on Zolgensma suggest that the gene therapy has the potential to deliver large benefits through a one-time treatment. Unfortunately, at its current pricing, Spinraza far surpasses common thresholds for cost-effectiveness. Among the various companies that are now bringing gene therapies to market, Novartis has a real opportunity here to demonstrate both scientific and ethical leadership by setting the launch price of Zolgensma in line with the benefits patients will likely receive.”

February 2019, Evidence Report on Treatments for SMA

Innovation around payment

Viewpoint

June 5, 2018

Value-Based Pricing for Drugs Theme and Variations

Anna Kaltenboeck, MA¹; Peter B. Bach, MD²

» [Author Affiliations](#)

JAMA. 2018;319(21):2165-2166. doi:10.1001/jama.2018.4871

Table. Comparison of Value-Based Pricing and Adjacent Concepts

Concept	Definition	Rests on Existing Evidence of Benefit	Aligns Price With Benefit at Market Entry	Examples
Value-based pricing	Price of a drug set on the magnitude of its benefit	Yes	Yes	Pricing of dupilumab according to ICER value-based price
Indication-specific pricing	Drug price specific to each of its uses	Yes	Yes	Tisagenlecleucel sold at 2 different prices for 2 different cancer indications
Outcomes-based contracts	Manufacturer refunds or rebates payer when an agreed-upon outcome is unmet	No	No	Amgen agreement with Harvard Pilgrim to refund cost of evolocumab for treated patients who have a myocardial infarction while taking the drug
Mortgage pricing	Commits a payer to pay for expensive treatments over time	No	No	No known examples
Value-based insurance design	A health benefit design that reduces out-of-pocket expense for high-value medical care and treatments	Yes	No	Prime Therapeutics program to reduce copayment and increase amount dispensed for insulins; Pitney Bowes' initiative to reduce or eliminate cost sharing for statins and clopidogrel

Abbreviation: ICER, Institute for Clinical and Economic Review.

Research Report

Perspectives on Spinraza (Nusinersen) Treatment Study: Views of Individuals and Parents of Children Diagnosed with Spinal Muscular Atrophy

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Factors that influence treatment decisions: costs/insurance

- ▶ **“What happens if she doesn’t get the drug?[...] How far back are we going to regress? What happens if no insurance is ever guaranteed? What happens if we can’t pay for it?...That emotional rollercoaster of knowing she could get stronger and then not knowing what would happen off of it terrified us.” (Parent, SMA II)**
- ▶ **“The problem is I worry that down the line...if I say, ‘Hey insurance company, will you pay for my new wheelchair,’ and the insurance company says, ‘Well, why aren’t you getting Spinraza,’ and I say, ‘Well, because I don’t want to get Spinraza,’ and they’re like, ‘Well, we’re not going to pay for your new wheelchair because, theoretically, you wouldn’t be in a wheelchair if you took Spinraza.’” (Adult, SMAI III)**

Factors that influence treatment decisions: costs/insurance

- ▶ Time

- ▶ Length of time to get approval
- ▶ Time burden required to get regular injections and manage side effects
- ▶ Need for lifelong commitment to treatment

- ▶ Transportation/Travel

- ▶ “How’s it going to affect our life; there’s inconveniences with the extra doctors appointments that we already have and don’t necessarily want more of.”
(Adult, SMA II)
- ▶ “There’s a lot of hassle. First of all, my city where I live doesn’t have an administration site. I would have to travel in order to pursue it. I work full time, so I have a job and I only have a limited amount of time off...I don’t have money to pay someone to travel with me out of town and possibly get a hotel if I need it.”
(Adult, SMA III)

Disability Identity

- ▶ "I'm 40 years old, right...Based on my progression, what I can see, I've given myself 20 good years. If I took that 20 years and I put that towards Spinraza...then it would amount to about I think close to 8 million dollars, right. If I had 8 million dollars handed to me and someone said, "[name], you can either take Spinraza and you might be able to open the hell out of this Ziploc container...or you can take this 8 million dollars and get all the intended care you need to never have to fight to get a new wheelchair. You can swim in a pool. You can have an accessible home. You can go anywhere you want to go. You never have to worry about your van breaking down.' Everything that I could ever need that would help me stay healthy and independent, I could buy with this eight million dollars, right, over being able to open a Ziploc container really well. I would be more cured if I put 8 million dollars towards that than to this drug." (Adult SMA II)

Disability Identity

- ▶ **"To me, the priority is very medically driven...the cost, it really hurts me, it hurts people and it hurts our world because it's putting a value on the idea of a cure that really isn't really there...an overall idea of disability being so atrocious that being able to open a Ziploc container is more important than having a full life that you can engage with. " (Adult SMA II)**

Conclusions/Recommendations

- ▶ Innovative approaches are needed to price and assess value, of gene therapies
- ▶ Access and equity are key: we cannot make gene therapy something that is only available to the very wealthy or the highly insured
- ▶ Gene therapies for rare/disabling conditions will challenge long-held assumptions about cost-effectiveness calculations and values
- ▶ Patient/stakeholder engagement will be key to success
- ▶ If the industry does not come up with practical and pragmatic solutions, the government likely will (and already is in Europe)

Thank you!

hktabor@Stanford.edu

Luxturna and Retinal Dystrophy



- ▶ Approved in US in December 2017 for treatment of biallelic RPE65 mutation-associated retinal dystrophy in children and adults (affects 1,000-2,000 in US)
- ▶ Approved in the EU in December 2018
- ▶ First in vivo gene therapy approved by the FDA
- ▶ \$425,000 per eye; Institute for Clinical and Economic Review says should be 50-75% less
- ▶ “We believe it’s a scientific milestone, but that for the majority of patients being treated, the cost is not in line with what’s considered cost-effective,” ICER Chief Medical Officer David Rind said.
- ▶ One subretinal injection for each eye
- ▶ Priority Review, Breakthrough Therapy, Orphan Drug designations, and Spark received a Rare Pediatric Disease Priority Review Voucher