What We Value:

The Proposition Behind the Price

Zahra Al-Khateeb, Nandini Hadker, Jillian Godfrey Scaife, Gavin Miyasato and Herman Sanchez

Background & Rationale

The cost of healthcare seems to have become a daily part of our national discourse. The headlines about sky-rocketing drug prices and unsustainable healthcare spend are becoming ubiquitous. As partners to the life sciences industry, Trinity understands that developing innovative therapies is expensive. For every 'blockbuster' product, there are many more failed attempts that require immense time and resources. Thus, when innovative treatments for life-threatening diseases come to market, we celebrate their success, their scientific achievement, and the narrative of their journey against all the odds, risks and the expenses of drug development. On the other hand, from a societal perspective, we understand the need to question the sustainability of such high prices.

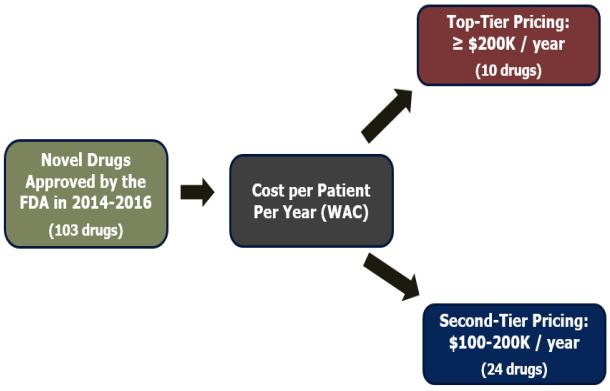
In writing this paper, we recognized that a disconnect exists between what we cherish as individuals and what we believe we can fund and support as a society. Projecting beyond our industry, it is no wonder then that we, as a society, seem to be struggling with our perspectives on medical breakthroughs in light of their costs.

This paper seeks to understand the interaction between value and price—ultimately asking:

What do the most expensive drug launches in the recent past reveal about what our society values? What does the market seem to be willing to pay for?

Methodology & Approach

In characterizing the relationship between cost and underlying value, we began with an empirical analysis of the costliest drugs approved between 2014-2016 using the FDA CDER's designated list of 'Novel Drugs'[1]. Excluding diagnostic imaging agents, we started with a list of 103 novel drug approvals. Price per patient per year for each treatment course was determined via RedBook® using WAC price at the time of approval and setting assumptions for weight-based dosing[2] and dosing duration and frequency.[3]



After costs were estimated, the list was separated into two pricing tiers: the *Top-Tier* consisted of the 10 products priced over $200,000 per patient per year, and the *Second-Tier* group containing the 24 products between $100,000-$200,000 per patient per year. Rather than analyze individual drugs, which can be subject to factors related to the individual product or disease area, we conducted our analysis at the Tier level to ask: **Even within some of the most expensive drug launches in the recent past, what factors appear to allow some drugs to price even higher (Top Tier) versus others (Second-Tier)?**

[1] CDER defines 'Novel Drugs' as products that were approved either as new molecular entities (NMEs) under New Drug Applications (NDAs), or as new therapeutic biologics under Biologics License Applications (BLAs)

[2] An average weight of 80 kg and 15 kg was assumed for adult and pediatric indications, respectively

[3] All treatments were costed out for duration within a given year; drugs for oncology indications whose dosing was specified as "until disease progression or unacceptable toxicity" were considered intermediate (vs. chronic or acute) and costed out assuming a patient was on treatment for the duration of a complete year

The tables below describe the Tier compositions.

Top-Tier Pricing: Products >$200K per patient per year, alphabetically by year of approval[4]

Product	Treatment Type	Indication	Rare Designation	Approval Year
Exondys 51	Chronic	Duchenne Muscular Dystrophy (DMD)	Yes	2016
Spinraza	Chronic	Spinal Muscular Atrophy (SMA)	Yes	2016
Cholbam	Chronic	Pediatric bile acid synthesis disorders	Yes	2015
Kanuma	Chronic	Lysosomal acid lipase (LAL) deficiency	Yes	2015
Orkambi	Chronic	Cystic Fibrosis (CF)	Yes	2015
Strensiq	Chronic	Hypophosphatasia (HPP)	Yes	2015
Cerdelga	Chronic	Adult Gaucher Disease, Type 1	Yes	2014
Cyramza	Intermediate	Advanced gastric cancer	Yes	2014
Myalept	Chronic	Leptin deficiency in lipodystrophy	Yes	2014
Vimizim	Chronic	MPS Type IVA (Morquio A syndrome)	Yes	2014

Second-Tier Pricing: Products $100-200K per patient per year, alphabetically by year of approval

Product	Treatment Type	Indication	Rare Designation	Approval Year
Lartruvo	Intermediate	Soft tissue sarcoma (Adult)	Yes	2016
Rubraca	Intermediate	Ovarian cancer	Yes	2016
Tecentriq	Intermediate	Bladder cancer	No	2016
Venclexta	Intermediate	Chronic lymphocytic leukemia	Yes	2016
Alecensa	Intermediate	ALK+ lung cancer	Yes	2015
Cresemba	Intermediate	Aspergillosis, mucormycosis	Yes	2015
Darzalex	Intermediate	Multiple myeloma	Yes	2015
Empliciti	Intermediate	Multiple myeloma	Yes	2015
Ibrance	Intermediate	Metastatic breast cancer	No	2015
Lenvima	Intermediate	Differentiated thyroid cancer (DTC)	Yes	2015
Natpara	Chronic	Hypoparathyroidism	Yes	2015
Ninlaro	Intermediate	Multiple myeloma	Yes	2015
Odomzo	Chronic	Local advanced basal cell carcinoma	No	2015
Portrazza	Intermediate	Advanced NSCLC	Yes	2015
Tagrisso	Intermediate	NSCLC	Yes	2015
Uptravi	Intermediate	Pulmonary arterial hypertension	Yes	2015
Xuriden	Chronic	Hereditary orotic aciduria	Yes	2015
Beleodaq	Intermediate	Peripheral T-cell lymphoma (PTCL)	Yes	2014
Keytruda	Intermediate	Metastatic melanoma	Yes	2014
Lynparza	Intermediate	Ovarian cancer	Yes	2014
Opdivo	Intermediate	Metastatic melanoma	Yes	2014
Sylvant	Intermediate	Multicentric Castleman's disease (MCD)	Yes	2014
Zydelig	Intermediate	Blood cancer	Yes	2014
Zykadia	Intermediate	Late-stage NSCLC	Yes	2014

[4] It is imperative to remember that "cost" of treatment, whether discussing the total cost of a drug per patient or to society, is driven by a myriad of factors—from the specificity of an individual patient's weight to the drug's route of administration and dosing schedule—all of which are subject to the vicissitudes of pharmaco/biologic treatment

Value Element Hypotheses

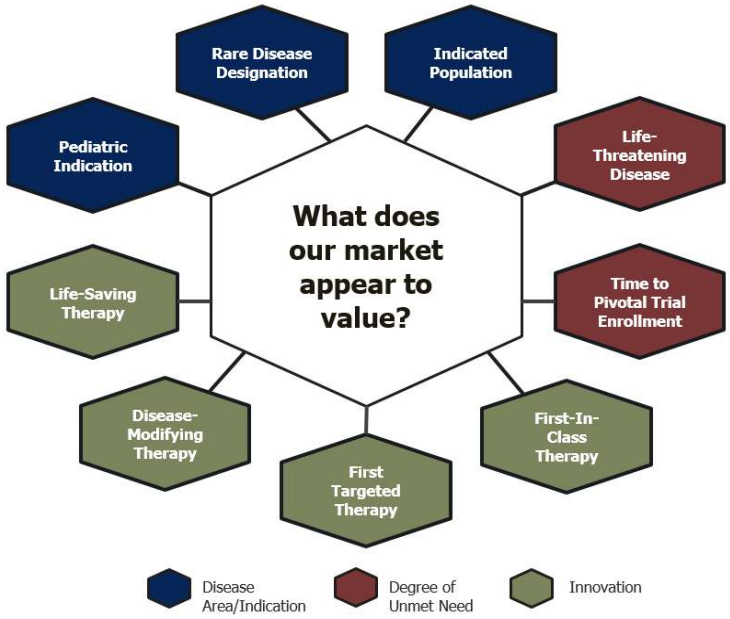
Each drug possesses its own value profile, with elements that address the disease population, unmet need and degree of innovation. We considered an array of hypotheses to test:

Disease area or indication:

- Was the drug for a **pediatric indication?**
  Do we have a greater willingness to accept cost when a treatment is for children?

- Was the drug for a **rare disease population[5]?**
  The Orphan Drug Act of 1983 was passed specifically to facilitate the development of orphan drugs to treat rare diseases through a number of incentives, including market exclusivity. Is willingness to pay higher when we are looking at a small, underserved population? Are patients with rare diseases and their advocacy groups more invested in drug development and launch, or do other factors/incentives come into play?

- What was the drug's **indicated population?**
  Do drugs targeting specific sub-groups or mutations garner more support as precision medicine continues to make its foray into the industry?



Degree of unmet need:

- Is the disease **life-threatening?** Life-shortening?
  Do we give greater priority to aggressively fatal conditions over long-term, debilitating ones?

- What was the **time to enrollment of the drug's pivotal trial – as a proxy for the level of unmet need?**
  Can time to enrollment be an indicator of unmet need? Are companies with drugs for 'more severe' diseases able to recruit patients faster for their clinical trials?

Innovation:

- Was the drug a **first-in-class therapy?[6]**
  Do we value scientific innovation and novel mechanisms of action?

- Was the **drug the first targeted therapy ever to launch for its disease?**
  Is our true measure of unmet need whether or not patients had any specific treatment options before this treatment?

- Was the drug a **disease-modifying therapy?**
  Do we distinguish and reward drugs that change the underlying etiology of a disease over those that manage symptoms?

- Was the drug a **life-saving therapy?**
  Do we demand proof of a drug's complete efficacy before we approve and/or pay for it?

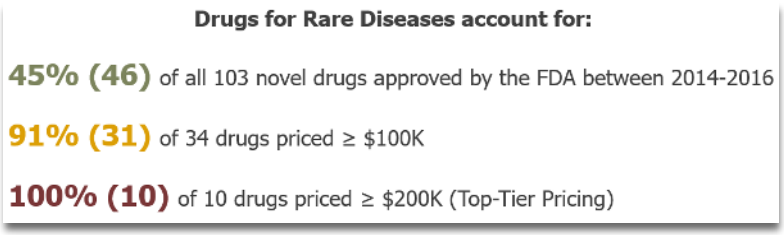
For this analysis, five metrics were chosen because of their definable and quantifiable nature: *Pediatric Indication, Rare Disease Designation, Indicated Incidence, First Targeted Therapy for Disease, and First-In-Class Therapy.* A review of the full list of hypotheses merits additional research and is planned for future publication.

[5] The FDA officially defines a rare disease as a disorder affecting *less than 200,000* people in the United States, as designated by the Rare Diseases Act in 2002
[6] The FDA officially defines first-in-class therapies as drugs with a new and unique mechanism for treating a medical condition

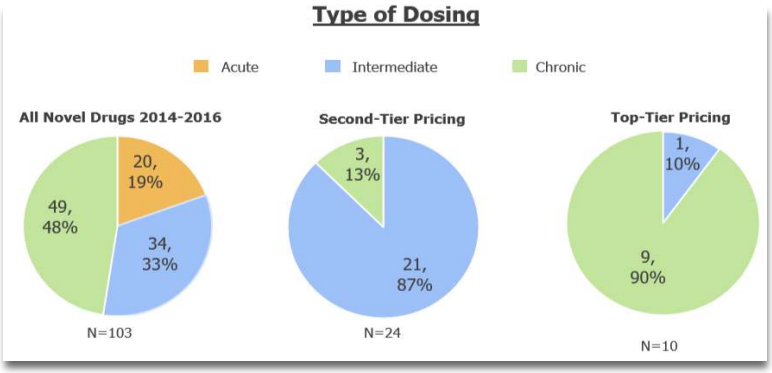
Value Characterization

5 key takeaways emerge from a holistic look at the data. The costliest drugs on a per-patient basis share several important traits:

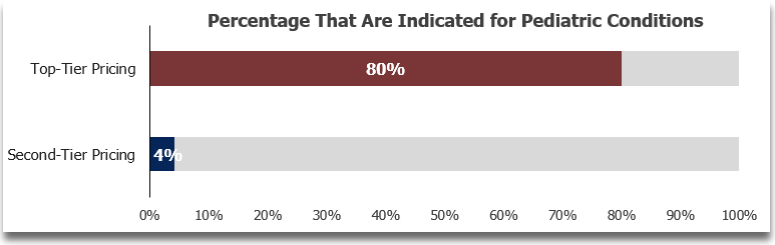
1) **Many of them address patients with Rare Diseases**



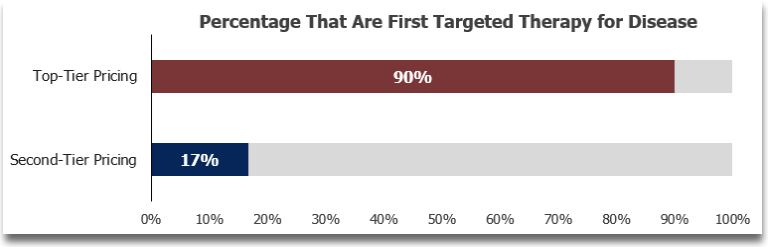
2) **Drugs requiring long-term, Chronic Dosing make up a disproportionate share of this list**



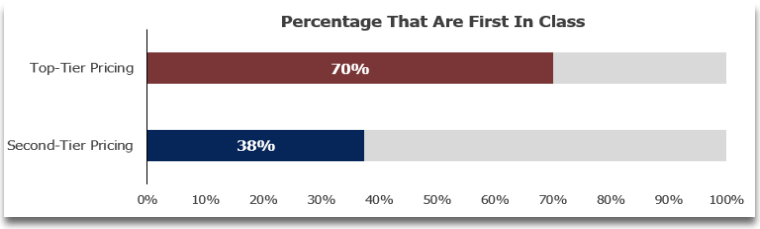
3) **The Top-Tier list is dominated by drugs for Pediatrics**



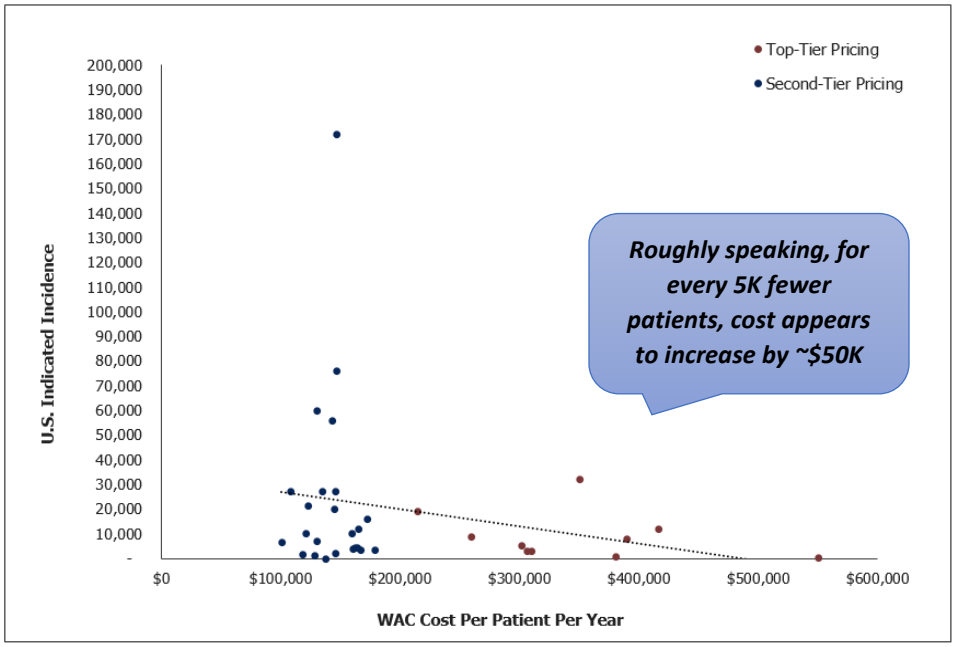
4) **The First Targeted Therapy for a Disease is very likely to be able to command top-dollar**



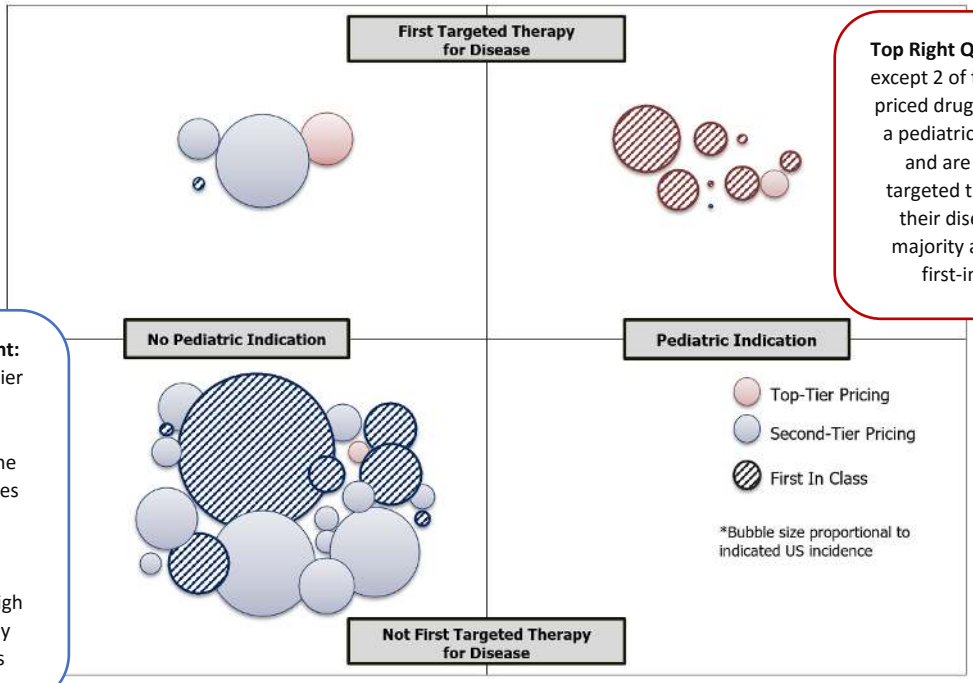
5) **Innovation matters: First-In-Class status gives you pricing leverage as well as access to Fast-Track Designation and other development mechanisms**



It is also important to note that most of these highly-priced drugs are not only rare, but have indicated yearly incidence rates of <30,000. Despite a degree of variation, higher **pricing appears to generally be in line with a lower indicated incidence.** While this could lead to multiple interpretations, two hypotheses come to mind: Manufacturers are having to spread R&D costs over a small patient pool, driving per patient costs higher. Concurrently, drug developers may be able to command higher prices because trials are more expensive and ultimately the **budget impact** to the payer is modest from a disease epidemiology perspective.



Analysis of the 34 Top-Tier and Second-Tier drugs from a multi-variate perspective, looking at clinical value as well as several indication-related dimensions, reveals several patterns summarized in the following bubble plot.



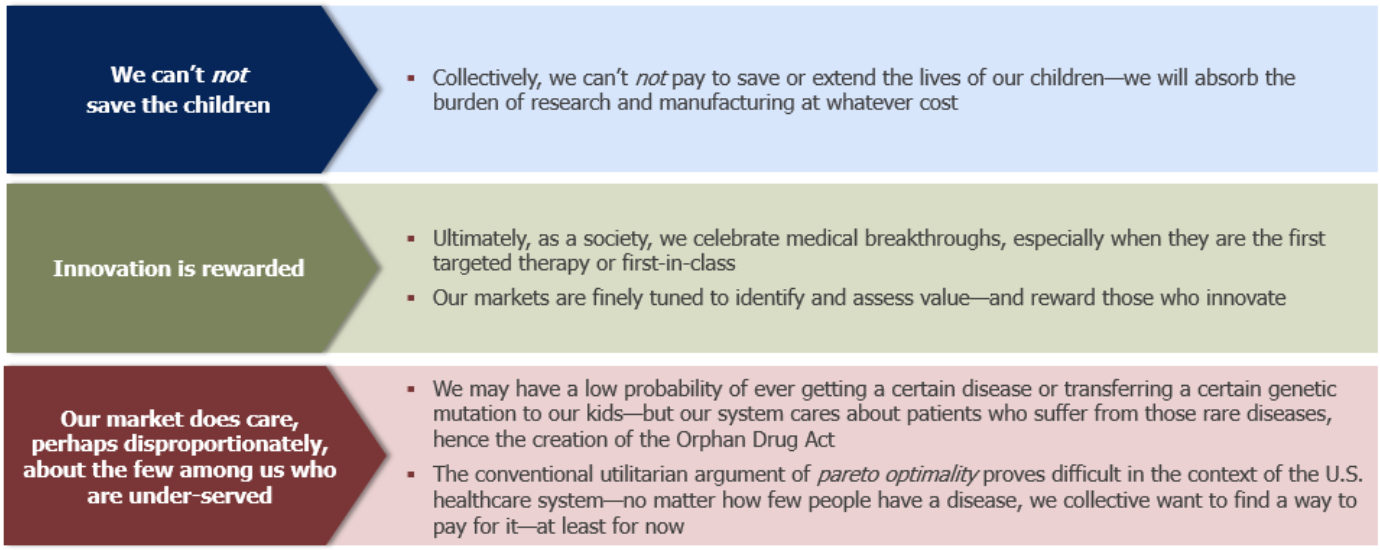
Top Right Quadrant: All except 2 of the Top-Tier priced drugs have both a pediatric indication and are the first targeted therapy for their disease, the majority also being first-in-class

Bottom Left Quadrant: Most of the Second-Tier priced drugs have NEITHER pediatric indications nor are the first targeted therapies for their diseases, however, they are primarily oncology products fulfilling a high unmet need in highly specific populations

As it turns out, many high-priced, rare disease drugs examined here have been expedited through the development process—whether due to the rarity of their indication and/or the urgency of finding an effective treatment. **Just under half of all the drugs priced >$100K per patient per year were granted Fast-Track Designation or Accelerated Approval by the FDA. 50% received Breakthrough Designation, and 30 out of the 34 in the analysis sample were given Priority Review status.** These mechanisms intended to expedite the arrival of new specialized therapies also mean that many drugs that have won recent approval have not completed confirmatory studies. Biogen released robust phase 3 data to support high-priced Spinraza (Top-Tier) several months after launch. Fortunately, the therapy did succeed in demonstrating clinically meaningful improvement in motor function. On the other hand, after much press surrounding its launch in bladder cancer, Roche's Tecentriq (Second-Tier) failed to meet its phase 3 endpoint several weeks post-approval. **These two examples do shed light on one additional factor that drives value creation: our healthcare system values *potential* —we are willing to pay for the promise of a useful treatment, even if it not fully vetted yet.**

Conclusions

Each and every drug included in the analysis above claims positive clinical data and a fulfillment of an important unmet need. Corresponding product websites emphasize the drugs' therapeutic and scientific value. How, then, can we distinguish what really matters with respect to drug pricing? The results of our analysis reveal several key findings about what our society values when it comes to new drug pricing:



The next question is: **How do we reconcile our microeconomic choices at the patient and disease level with our macroeconomic choices about how much budget to allocate to healthcare spend, and what exactly to prioritize?** Thinking about this as a theoretic construct, should we as a society seek to improve *everyone's* health by 10%, or should we allocate that same budget to potentially improve or save the lives of a few? Who gets to decide?

While these ethical and philosophical questions warrant further deliberation, as healthcare consultants living in today's world, we need to help our clients in the immediate- and short-term. We need to help them navigate the uncertainty of the review, approval and reimbursement process and build an evidentiary pathway for their product to succeed. We need to help them identify the key metrics for success within a disease area, clarify and communicate their drug's value proposition, and develop compelling health economic evidence to support the path to market—with the knowledge that the question of price is likely to only grow in sensitivity.

Our industry will likely continue to evolve in the coming years, and several key questions remain. Will payers continue to reward innovation – no matter the overall cost? What evidence will they demand and what barriers, if any, will they place on utilization? Will payers continue to make piece-meal decisions about individual rare diseases, or will they start to think about rare diseases collectively and begin to push back?

If this research has taught us anything, it is to continue to ask these questions—and to continue to push for answers.