TRINITY

WHITE PAPER

Trinity Annual Drug Index

Evaluating the Commercial Performances of Novel Drugs Approved in 2020

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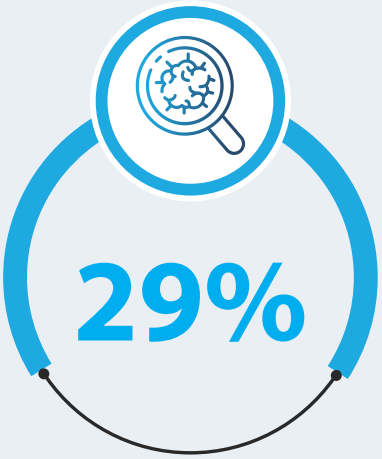
Introduction

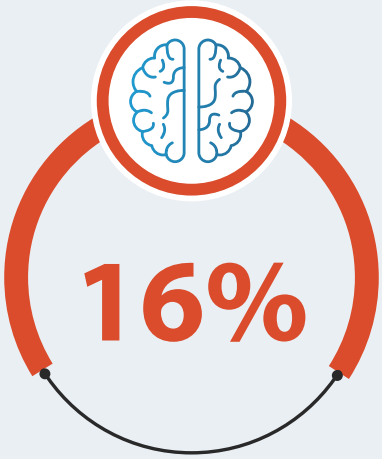
This report, the sixth in our Trinity Drug Index series, outlines key themes and emerging trends in the industry as we progress towards a new world of targeted and innovative products. We provide a comprehensive evaluation of the performance of novel drugs approved by the FDA in 2020, scoring each on its commercial performance, therapeutic value and R&D investment (Table 1: Drug ranking – Ratings on a 1-5 scale). 2020 saw 58 unique drug and biologic approvals, of which the majority were Oncology (29%) followed by Neurology (16%). In this report we describe the notable themes and trends within the industry and take a deeper look into a few products with outstanding performance. The COVID-19 pandemic, which swept the globe in 2020, brought unprecedented challenges and disruptions to the pharmaceutical industry, reshaping priorities and accelerating research efforts towards finding innovative solutions.

2020 FDA Approvals

unique drug and biologic approvals



of approvals were Oncology



of approvals were Neurology

Key Highlights

1. The Performance of FDA-Approved Products in 2020, Particularly Intravenous (IV) Products, Was Notably Impacted by the Challenges Brought About by the COVID-19 Pandemic

The COVID-19 pandemic had a profound impact on the pharmaceutical industry in 2020. There was a significant shift of priorities, with a greater portion of R&D efforts focused on the development of vaccines, treatments and therapies for the virus. Additionally, supply chain disruptions, clinical trial delays and shifts in healthcare utilization patterns, including but not limited to restricted access to healthcare facilities, posed challenges for the industry. As a result, products launched in 2020 performed commercially worse than they should have. Figure 1 highlights the impact of the pandemic as products launched in 2020 result in a flatter linear regression line (blue line) when compared to products launched between 2016-2019, suggesting that products with similar therapeutic scores netted better commercial scores in previous years. **Only the products that were very strong therapeutically or were addressing significant unmet need were able to perform commercially.**

2. Oncology and Neurology Continue to Lead Indications in 2020

2020 saw a return to "normalcy" for the number of drugs approved within the Oncology space, sharply increasing to ~29% (17/58) of new approvals in 2020 – up from ~23% (12/53) in 2019 and in-line with ~25% (16/65) in 2018. Meanwhile, 2020 saw a slight decrease in the number of drugs approved within the Neurology space, decreasing to ~16% (9/58) in 2020 – down from ~23% (12/53) in 2019, but up from ~6% (4/65) and ~11% (6/56) in 2018 and 2017, respectively. Collectively, **Oncology and Neurology indications combined have continued to command a greater proportion of the approved therapies**, increasing from ~34% in 2017 to ~45% in 2020. Of the 17 drugs approved for Oncology indications, just over half (9/17) were small molecules and ~24% were monoclonal antibodies. Additionally, one of the two approved antibody drug conjugates (ADCs) this year, (TRODELVY®), was the highest performing Oncology drug overall, and manufacturer Gilead would also go on to acquire the only CAR-T approved this year (TECARTUS®). Of small molecule approvals, two-thirds of the products were mutation-directed, compared with only 25% (1/4) of the monoclonal antibodies.

3. Companies that Launched Their First Products Continued to Struggle to Meet Forecast Expectations

~21% (12/58) of approved products in 2020 constituted a "first launch" for their respective companies, a slight uptick from ~15% (8/53) in 2019. Of the "first launch" products, ~42% (5/12) were approved for Oncology including QINLOCK® (Deciphera Pharmaceuticals), MARGENZA® (MacroGenics), MONJUVI® (MorphoSys), AYVAKIT® (Blueprint Medicines) and TAZVERIK® (Epizyme), while ~17% (2/12) were approved for Neurology indications including VILTEPSO® (Nippon Shinyaku) and OLINVYK® (Trevena). ~17% (2/12) of "first launch" drugs were also launched in Cardiology and Gastroenterology indications each. **None of the "first launch" products in 2020 surpassed their forecast expectations** (compared to only one, OXBRYTA®, in 2019), while ~50% significantly underperformed (<32% of forecast expectations). Like 2019, none of the top ten highest scoring products in 2020 were "first launch" products. **Non-"first launch" products performed similarly to 2019** (see Figure 2), highlighting the advantage companies with established commercial capabilities possess.

Drug Ranking

The overall and component scores for each drug are shown in Table 1. As with each of the prior Trinity Drug Indices, the three component scores for each of the products were informed by an internal survey of Trinity leadership and management to assess therapeutic value, an analysis of expected versus actual revenue to assess commercial performance and an analysis of length and size of clinical trials to assess R&D investment. Component scores were combined into the overall score in the following proportions: 40% commercial score, 40% therapeutic score and 20% R&D score.

Table 1: Drug Ranking – Ratings on a 1-5 Scale (Higher scores indicate better performance)[1]

Brand Name (Company)	Therapeutic Area Approval	2020 Indication Approval[1]	FDA Approval Date	Reported Revenue in 2020 ($M)	Reported Revenue in 2021 ($M)	Component Scores			Overall Score
						Therapeutic Score	Commercial Score	R&D Score	
TEPEZZA® (Horizon Therapeutics)	Ophthalmology	TED	1/21/2020	$820.0	$1,661.2	4.2	4.6	3	4.1
NURTEC ODT® (Biohaven[2] / Pfizer)	Neurology	Migraine	2/27/2020	$0.0	$462.5	4	4	2.5	3.7
TRODELVY® (Gilead Sciences)	Oncology	Breast Cancer	4/22/2020	$49.0	$370.0	4.2	3.6	2.5	3.6
EVRYSDI® (Roche)	Neurology	Spinal Muscular Atrophy	8/7/2020	$58.7	$399.5	4.2	3	3	3.5
TECARTUS® (Gilead Sciences)	Oncology	Mantle Cell Lymphoma (MCL)	7/24/2020	$34.0	$136.0	4.2	2.4	4	3.4
PEMAZYRE® (Incyte)	Oncology	Cholangiocarcinoma	4/17/2020	$25.9	$53.5	4.8	1.4	4	3.3
OXLUMO® (Alnylam Pharmaceuticals)	Nephrology	Hyperoxaluria Type 1	11/23/2020	$0.0	$0.0	4.8	1.2	4	3.2
KOSELUGO® (AstraZeneca)	Neurology	Neurofibromatosis Type 1	4/10/2020	$38.0	$104.0	4.8	2.2	2	3.2
TUKYSA® (Seagen)	Oncology	HER2+ Breast Cancer	4/17/2020	$119.6	$280.1	4	3.2	1.5	3.2
RETEVMO® (Eli Lilly)	Oncology	RET+ NSCLC	5/8/2020	$36.5	$99.4	4	1.6	4.5	3.1
ZEPOSIA® (Bristol Myers Squibb)	Neurology	Relapsing Forms of Multiple Sclerosis	3/25/2020	$0.0	$6.6	3.8	1.4	5	3.1
ORLADEYO® (BioCryst Pharmaceuticals)	Hematology	Hereditary Angioedema	12/3/2020	$0.0	$122.6	3	2.6	4	3.0
ZEPZELCA® (Jazz Pharmaceuticals)	Oncology	SCLC	6/15/2020	$90.4	$246.8	3.2	3	2.5	3.0
DOJOLVI® (Ultragenyx Pharmaceutical)	Metabolic	Long-Chain Fatty Acid Oxidation Disorders	6/30/2020	$8.6	$29.8	4.2	1.4	3.5	2.9
DANYELZA® (Takeda)	Oncology	Neuroblastoma	11/25/2020	$0.0	$0.0	5	1.4	1.5	2.9
ORGOVYX® (Sumitomo Pharma)	Oncology	Prostate Cancer	12/18/2020	$0.0	$0.0	3.8	1.8	3	2.8
TABRECTA® (Novartis)	Oncology	NSCLC	5/6/2020	$6.0	$79.3	4.4	1.4	2.5	2.8
ZOKINVY® (Eiger BioPharmaceuticals)	Cardiology	Premature Aging	11/20/2020	$0.0	$12.1	3.8	1.4	3.5	2.8
VILTEPSO® (Nippon Shinyaku)	Neurology	Duchenne Muscular Dystrophy	8/12/2020	$3.7	$32.9	3.2	1.2	5	2.8
GEMTESA® (Sumitomo Pharma)	Genito-Urinary	Overactive Bladder	12/23/2020	$0.0	$63.3	3.8	1.8	2.5	2.7

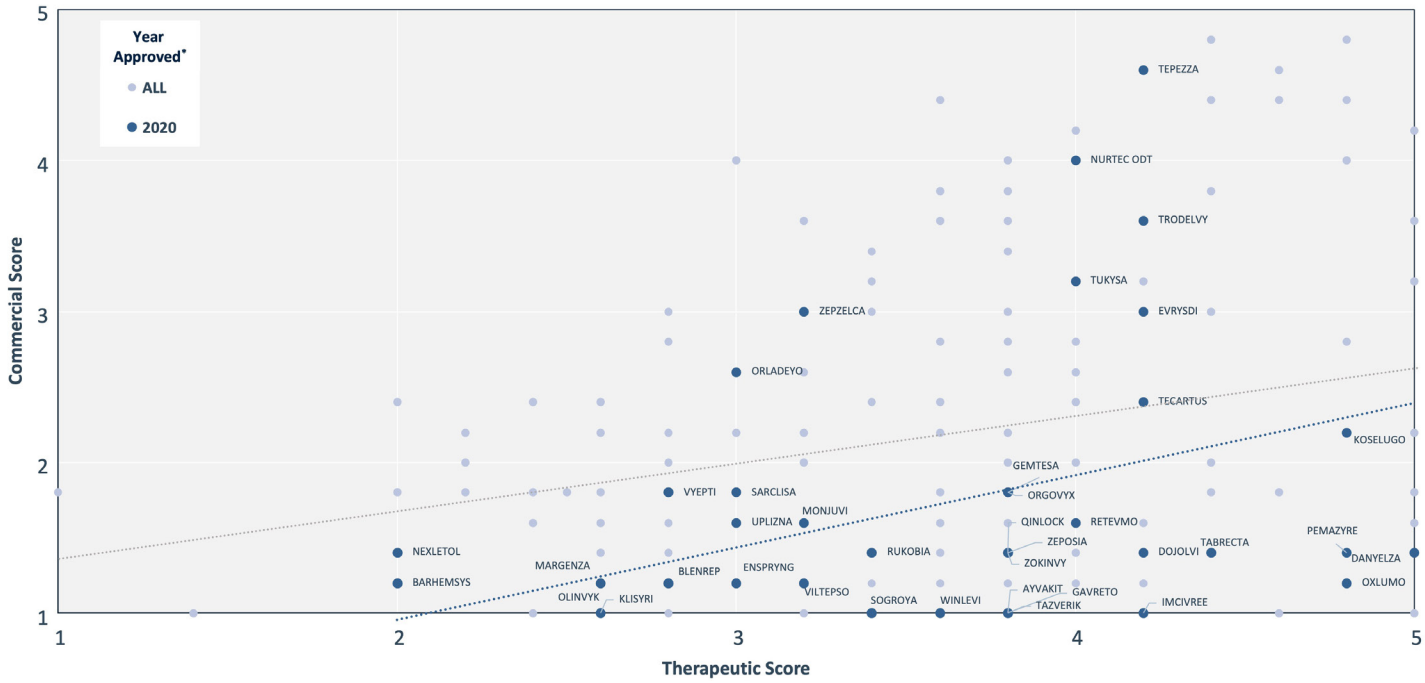
[1] Certain products in multi-year analysis have been approved for multiple indications since initial approval in 2020. As such, we have indicated the first indication approvals. Certain products were also omitted from the analysis due to limited financial data. Please note that this applies to the following 2020 products: **EBANGA®, INMAZEB®, LAMPIT®, ARTESUNATE®, ISTURISA®, ONGENTYS®, PALFORZIA®, PIZENSY®, SEVENFACT® and XEGLYZE®. VEKLURY®** was also omitted from the analysis due to skew in its commercial sales driven by the COVID-19 pandemic

Brand Name (Company)	Therapeutic Area Approval	2020 Indication Approval[1]	FDA Approval Date	Reported Revenue in 2020 ($M)	Reported Revenue in 2021 ($M)	Component Scores			Overall Score
						Therapeutic Score	Commercial Score	R&D Score	
UPLIZNA® (Horizon Therapeutics)	Neurology	NMOSD	6/11/2020	$8.0	$60.8	3	1.6	4	2.6
TAZVERIK® (Epizyme)	Oncology	Sarcoma	1/23/2020	$3.8	$10.2	3.8	1	3.5	2.6
MONJUVI® (MorphoSys)	Oncology	DLBCL	7/31/2020	$21.1	$79.2	3.2	1.6	3	2.5
RUKOBIA® (GSK)	Infectious Disease	HIV	7/2/2020	$14.1	$59.2	3.4	1.4	3	2.5
GAVRETO® (Roche)	Oncology	NSLC	9/4/2020	$0.0	$8.2	3.8	1	3	2.5
ENSPRYNG® (Roche)	Neurology	NMOSD	8/14/2020	$6.4	$25.2	3	1.2	4	2.5
QINLOCK® (Deciphera Pharmaceuticals)	Oncology	Gastrointestinal Stromal Tumor (GIST)	5/15/2020	$38.0	$81.5	3.8	1.4	2	2.5
IMCIVREE® (Rhythm Pharmaceuticals)	Gastroenterology	Obesity Associated with Pro-Opiomelanocortin Deficiency	11/25/2020	$0.0	$0.0	4.2	1	2	2.5
SOGROYA® (Novo Nordisk)	Endocrinology	Growth Hormone	8/28/2020	$0.0	$0.0	3.4	1	3.5	2.5
KLISYRI® (Almirall)	Dermatology	Actinic Keratosis	12/14/2020	$0.0	$4.7	2.6	1	5	2.4
BLENREP® (GSK)	Oncology	Multiple Myeloma	8/5/2020	$32.1	$84.0	2.8	1.2	4	2.4
VYEPTI® (Lundbeck)	Neurology	Migraine	2/21/2020	$14.2	$78.3	2.8	1.8	2.5	2.3
AYVAKIT® (Blueprint Medicines)	Oncology	Gastrointestinal Stromal Tumor (GIST)	1/9/2020	$20.5	$26.7	3.8	1	2	2.3
SARCLISA® (Sanofi)	Oncology	Multiple Myeloma	3/2/2020	$29.7	$79.3	3	1.8	1.5	2.2
WINLEVI® (Cassiopea)	Dermatology	Acne	8/26/2020	$0.0	$19.6	3.6	1	1	2.0
MARGENZA® (MacroGenics)	Oncology	HER2+ Breast Cancer	12/16/2020	$0.0	$12.3	2.6	1.2	2	1.9
BARHEMSYS® (Acacia Pharma)	Gastroenterology	Prevent Nausea and Vomiting after Surgery	2/26/2020	$0.0	$7.1	2	1.2	3	1.9
OLINVYK® (Trevena)	Neurology	Acute Pain	8/7/2020	$0.1	$0.5	2.6	1	2	1.8
NEXLETOL® (Esperion Therapeutics)	Cardiology	Heterozygous Familial Hypercholesterolemia	2/21/2020	$13.0	$40.0	2	1.4	1	1.6

[2] NURTEC ODT® is now owned by Pfizer.

Figure 1. Comparison of Therapeutic and Commercial Scores for Drugs Approved by the FDA, 2020

The line below is the linear regression of commercial score on therapeutics score for drugs approved by the FDA and included across all drugs approved in 2020, relative to the rest of the Drug Indices from 2016-2019.



*Includes products reviewed in previous Trinity Drug Indices from 2016-2019

Figure 2. Comparison of Commercial Performance by Product Type in 2019 vs 2020: "First Launch" Product for Company vs Not First Launch for Company

Commercial performance compared forecasted sales over the first two years post-launch to the actual sales. In other words, how is the drug doing compared to expectations?

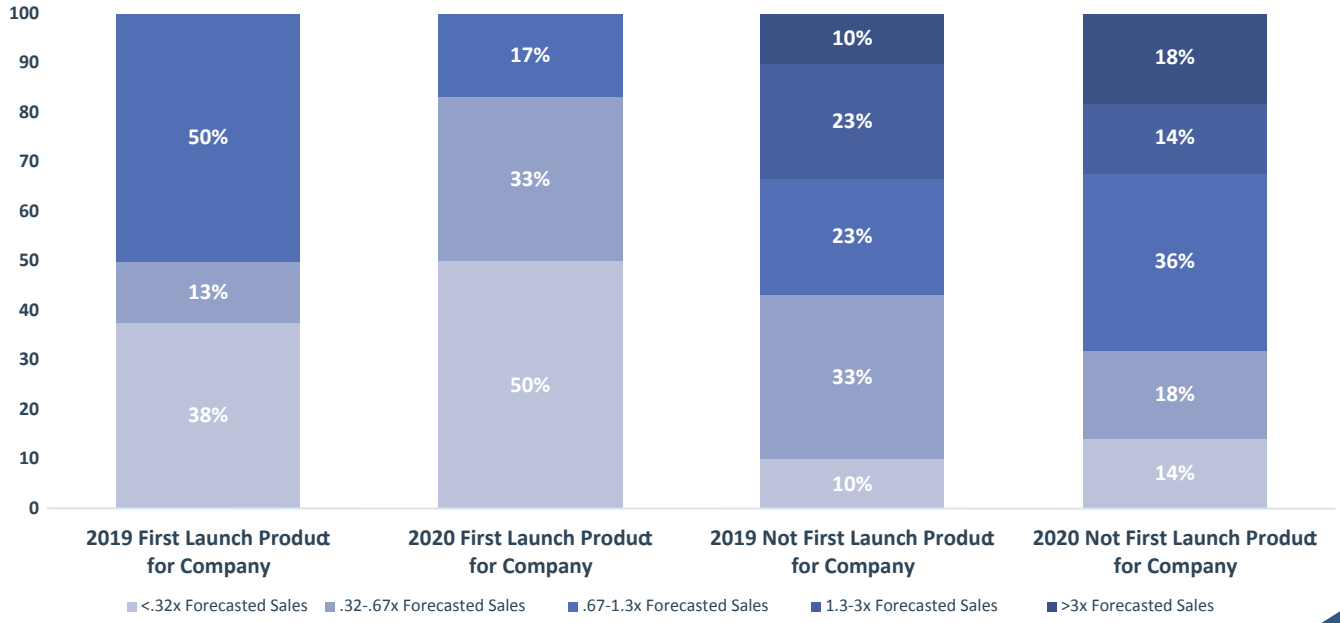
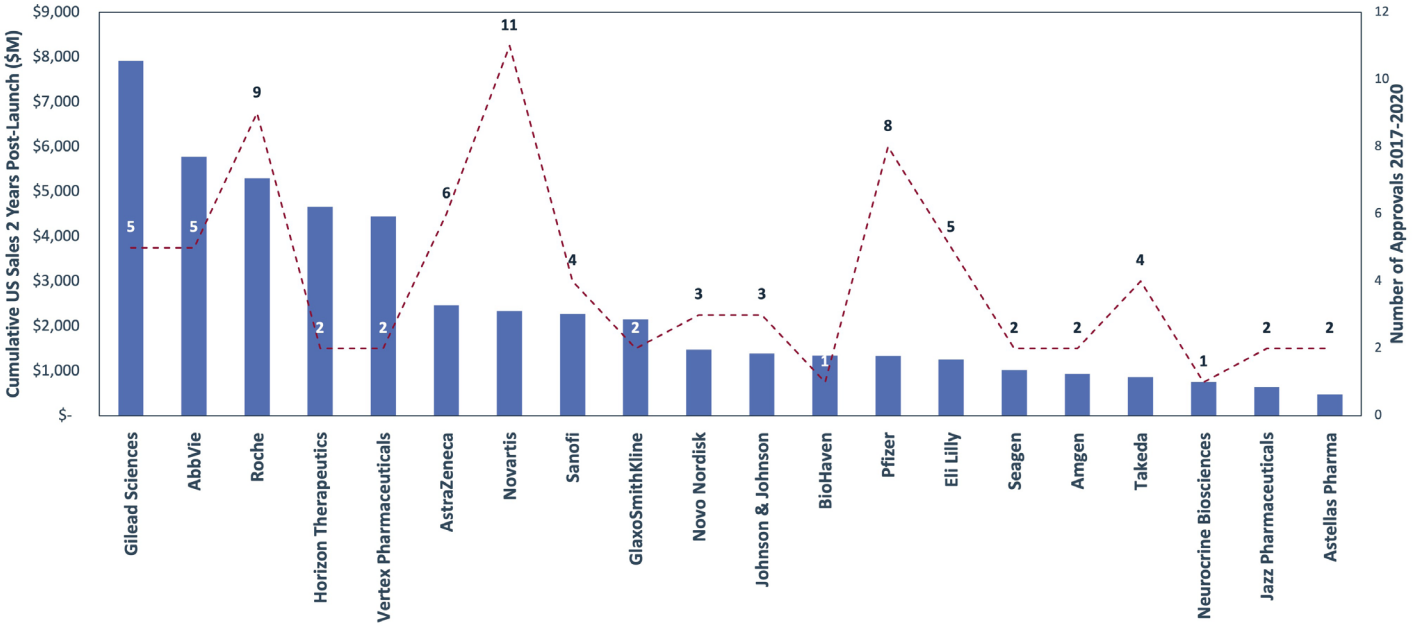


Figure 3. Comparison of Cumulative U.S. Sales of New Drug Launches for Top 20 Companies 2017-2020

Actual U.S. sales over the first two years post-launch were summed for companies with drug launches 2017-2020, overlayed with the number of drug launches over the same period.



Key Themes

COVID-19 Resulted in Fewer Drugs Following the Relationship Between Therapeutic Value Leading to Material Commercial Performance, Particularly Intravenous (IV) Products

Compared to prior years, the therapeutic score of drugs approved in 2020 had a weaker relationship with the commercial score. Drugs that **did not provide a significant value proposition** (i.e., entering crowded markets without differentiating attributes, me-too drugs, etc.) **were significantly impacted by the pandemic and commercially underperformed** relative to what would be expected based on their therapeutic score (see Figure 1). The only drugs that performed well on the commercial axis in Figure 1, TEPEZZA®, NURTEC ODT®, TRODELVY®, TUKYSA® and EVRYSDI®, all brought significant innovation and were launching into high unmet need indications. Many drugs that rated a 4 or greater on the therapeutic axis in Figure 1, including DANYELZA®, OXLUMO® and PEMAZYRE®, were below the linear regression line. Only two drugs, ZEPZELCA® and ORLADEYO® were materially above the linear regression line in 2020 despite having a therapeutic score less than 4.

Additionally, while 2020 saw a marked increase in total number of approved products, the average commercial score and therapeutic scores (Table 1: Drug ranking – Ratings on a 1-5 scale) were considerably lower than the average seen from 2017-2020, especially for drugs with an injection route of administration (ROA), i.e., intravenous infusion or subcutaneous injection. Drugs with an IV route of administration performed ~12% and ~14% worse on the commercial and therapeutic scores, respectively, than the 4-year average, while drugs with an oral ROA performed ~3% and 18% worse on the commercial and therapeutic scores, respectively, than the 4-year average. While average cumulative U.S. sales two-years post launch for 2020 were in-line with previous years, the average cumulative U.S. forecasted sales three to seven years post launch were materially lower for 2020 compared to previous years. Once again, this highlights the impact COVID-19 had on the commercialization prospects on drugs launching in 2020, especially among IV therapies that required patients to go in-person for treatment. It will be important to analyze if this trend continues in products launched in subsequent years (to be determined in future Trinity Drug Indices) and in the long-term performance of the drugs launched in 2020.

Few Diamonds in the Rough

Though small-to-mid cap companies (SMID) companies/those launching their first product typically fare worse than big pharma, **the top two highest cumulative U.S. sales two years post-launch in 2020 were from SMID companies, Horizon Therapeutics** (TEPEZZA® and UPLIZNA®; $6.5B[3] market cap at launch of TEPEZZA in January) **and Biohaven** (NURTEC ODT®; $2.6B[3] market cap at launch of NURTEC ODT in February). This was an outlier year compared to prior years with big pharma leading the way: in 2017 Roche (HEMLIBRA® and OCREVUS®) and GSK (SHINGRIX®); in 2018 Gilead (BIKTARVY®) and Takeda (TAKHZYRO®); in 2019 AbbVie (SKYRIZI®, RINVOQ® and UBRELVY®) and Vertex (TRIKAFTA®). Ultimately, this resulted in both companies being acquired: Pfizer agreed to acquire Biohaven in May 2022 for $11.6B[4] and Amgen agreed to acquire Horizon Therapeutics in December 2022 for $27.8B.[5]

Looking over 2017-2020, **only Horizon breaks into the top ten of cumulative U.S. sales two years post-launch** (see Figure 3), highlighting the need for a significant value proposition (i.e., high unmet need disease, first disease-modifying product for indication, meaningful change in route of administration and/or dosing frequency) in order to convert into a successful launch. Big pharma companies that have been successful over this period tended to launch at least four drugs in order to cumulatively post significant gross sales: Roche (9 new drug launches) and Novartis (11 new drug launches). Other big pharma, such as Pfizer (8 drug launches) and Eli Lilly (5 new drug launches), have realized lower revenue, partially driving M&A activity (i.e., Biohaven and Seagen for Pfizer, Loxo Oncology, Dice Therapeutics and Dermira for Eli Lilly, among others).

[3] Market cap for Horizon Therapeutics and Biohaven were calculated by multiplying share price with the amount of outstanding shares in January 30 and February 27, respectively

[4] https://www.pfizer.com/news/press-release/press-release-detail/pfizer-acquire-biohaven-pharmaceuticals

[5] https://www.amgen.com/newsroom/press-releases/2023/10/amgen-completes-acquisition-of-horizon-therapeutics-plc

Case Studies

The Trinity team performed two sets of case studies to elucidate perspectives for driving commercial success. In the first set of case studies, two indications with two novel product approvals, Neuromyelitis Optica/ Neuromyelitis Optica Spectrum Disorders (NMOSD) and Metastatic Gastrointestinal Stromal Tumor (GIST), were analyzed to compare the outcomes based purely on the product's clinical profile and the manufacturer's ability to successfully commercialize. In the second set of case studies, the top four ranked drugs were profiled based on their therapeutic, commercial and R&D score. For each drug, the context and use of the drug, its commercial performance and learnings are illustrated.

NMOSD: UPLIZNA® and ENSPRYNG®

Background: NMOSD is an autoimmune central nervous system (CNS) disease that primarily attacks the optic nerves and spinal cord, leading to blindness and paralysis. RITUXIN® (rituximab) and SOLIRIS® (eculizumab) are most frequently used, with SOLIRIS® being reserved for severe patients or those who relapse on RITUXIN®. UPLIZNA® (Horizon Therapeutics) and ENSPRYNG® (Roche) launched in June and August 2020, respectively, for adult NMOSD patients who are anti-aquaporin-4 (AQP4) antibody positive. UPLIZNA® is a CD19-directed cytolytic antibody, while ENSPRYNG® is an interleukin-6 receptor antagonist.

Results: Though both products launched close to one another and ENSPRYNG® was supported by the wide spanning commercial capabilities of Roche, UPLIZNA® has become the number three biologic option for AQP4+ NMOSD patients. The primary driver for the difference in utilization was the clinical profile: ENSPRYNG® is both less efficacious than UPLIZNA® (which is itself less efficacious than SOLIRIS®) and less convenient dosing schedule compared to UPLIZNA® (subcutaneous (SC) every four weeks vs. intravenous (IV) infusion every six months). Furthermore, ENSPRYNG® has the added safety concerns of increased risk for infection that is potentially fatal. Through 2020-2022, UPLIZNA® and ENSPRYNG® have generated ~$223 million and ~$88 million, respectively, and are forecasted to generate ~$1,600 million and ~$870 million 2023-2027.

Commercial Learnings: Despite launching into a crowded market (with additional entrants including ULTOMIRIS® (ravulizumab)), **UPLIZNA® addressed key unmet needs and differentiation points** in order to establish a meaningful piece of the NMOSD market. Relative differences in sales outcomes also highlight the necessity of new products to nail the basics (i.e., efficacy similar to or better than standard of care (SOC) without introducing additional safety risk) before adding in bells and whistles (i.e., SC vs. IV dosing), especially in high unmet need indications like NMOSD.

> "Despite launching into a crowded market, UPLIZNA® addressed key unmet needs and differentiation points in order to establish a meaningful piece of the NMOSD market."

Case Studies

GIST: AYVAKIT® and QINLOCK®

Background: GIST is a rare solid tumor malignancy that originates in the gastrointestinal (GI) tract. It represents a small proportion of tumors affecting the GI tract and is commonly observed in individuals aged 50 years and older. GLEEVAC® (imatinib), SUTENT® (sunitinib) and STIVARGA® (regorafenib), all tyrosine kinase inhibitors (TKIs), have long been the most commonly used treatments for metastatic patients. In January 2020, Blueprint Medicines launched AYVAKIT®, and four months later Deciphera Pharmaceuticals introduced QINLOCK®. AYVAKIT® and QINLOCK® are both TKIs, specifically targeting mutations in the KIT and PDGFRA genes, which are known to drive the growth of GISTs. Despite the similarity in their mechanism, the FDA approved these products with different GIST indications: QINLOCK® to treat patients after three or more prior lines and AYVAKIT® to treat PDGFRA exon 18 mutant patients of any line.[6]

Results: AYVAKIT® and QINLOCK® have generated ~$83 million and ~$217 million, respectively, over the last three years and are forecasted to generate ~$222 million and ~$614 million over the course of the next five years (2023-2027). With back-to-back approvals within the same solid tumor, **AYVAKIT® and QINLOCK® may appear to be direct competitors, but in practice they have effectively played in two distinct, yet interrelated spaces.** As the first approved biomarker-directed therapy, AYVAKIT® has created a new niche within the GIST market and is now preferred for first line use, ahead of long entrenched GLEEVEC®, in the subset of patients who harbor a PDGFRA exon 18 mutation. However, this only constitutes ~6% of all GIST patients. QINLOCK®, on the other hand, is approved for use in fourth line or later patients, irrespective of biomarker status, and has subsequently captured a significant proportion of patients who have exhausted all prior standard of care options. With a failed AYVAKIT® trial in third line or later all-comers against STIVARGA®, it appears these products will continue to play alongside each other in parallel subsets of the GIST market, with revenue potential for AYVAKIT®'s heavily dependent upon the uptake of biomarker testing.[6] However, given how commonplace early and broad biomarker testing has become for oncologists across a number of solid tumors, eligible patient identification for AYVAKIT® should continue to improve.

Commercial Learnings: AYVAKIT® and QINLOCK® demonstrate how different types of label restrictions can impact commercial potential within a high unmet need market. Despite a seemingly broader label without prior line restrictions, AYVAKIT® is limited by the small proportion of GIST patients who harbor a PDGFRA exon 18 mutation. In a therapeutic area like oncology that is moving increasingly toward precision medicine and personalized treatments, these two cases indicate the tradeoff between providing significant value to a small subset of patients and providing incremental value to a larger pool of patients.

[6] As of March 2023, NCCN guidelines were updated to include QINLOCK® as a preferred regimen for second-line GIST patients intolerant to Sunitinib based on results of the phase III INTRIGUE trial. FDA has granted breakthrough therapy designation, and Deciphera initiated the pivotal INSIGHT trial in November 2023 to potentially enable label expansion to second line patients with certain KIT mutations.

> "AYVAKIT® and QINLOCK® may appear to be direct competitors, but in practice they have effectively played in two distinct, yet interrelated spaces."

Case Studies

TEPEZZA® Case Study: (Drug of the Year)

Background: Prior to the launch of TEPEZZA® in early 2020, there were no approved treatments available for thyroid eye disease (TED), a rare autoimmune condition causing inflammation and swelling around the eyes that can eventually become sight-threatening. Approximately 15-20K new moderate-severe patients develop TED in the U.S. each year, whose only prior options featured off-label immunologic agents (e.g., glucocorticoids, MMF, Rituxan, Actemra). Like many rare diseases, TED is commonly misdiagnosed given its heterogeneous presentation, various differential diagnoses (e.g., dry eye, conjunctivitis) and rapid fluctuation between active and chronic phases. As the first labeled TED treatment, TEPEZZA® addresses the root cause of the disease, binding to the receptors in the cells behind a patient's eyes to effectively block the "switches" that turn on the tissue swelling characteristic of the disease.

Results: With approximately six weeks on the market in early 2020 prior to COVID-19-induced global shutdowns, Horizon was able to rapidly deploy its field force to establish an early presence at physician offices. TEPEZZA® was able to swiftly surpass prior sales projections, which significantly underestimated the size of the eligible patient pool and the degree to which TEPEZZA® could activate treaters and identify patients. Despite the global pandemic, **Horizon saw TEPEZZA® garner just under $1B sales in its first year,** with eventual peak sales expected to roughly triple as patient identification continues to improve. However, TEPEZZA® has lost some of its momentum in 2023 after posting an 8% decline year-over-year in third quarter. Part of this may be due to the bullish uptake TEPEZZA® achieved at launch given the unexpected size and urgency of the prevalent patient bolus TEPEZZA® was able to immediately tap into, and part of it may be the low level of awareness for the disease in milder/less urgent patients. Amgen is working to leverage its sales team that cover endocrinologists to broaden awareness of TEPEZZA®. Additionally, there is also potential for additional growth following an FDA label expansion in April, which has already led to a 50% year over year increase in TEPEZZA® prescribers.[7]

Commercial Learnings: Horizon's early engagement of both patients and payers supported its strategy of establishing a presence at a small network of centers of excellence (COEs) before expanding for broader reach. The variety of digital promotional materials Horizon generated to support TEPEZZA®'s launch, including unbranded campaigns heightening disease awareness prior to launch, positioned the company well to at least partially mitigate the impact of COVID-19. By initially establishing its presence at key COEs with endocrinologists and ophthalmologists, Horizon was able to gain a foundational foothold for TEPEZZA®. Assembling a multi-disciplinary TED expert network facilitated the broader consolidation of diagnosis and treatment practices outside of these limited centers. Consequently, TEPEZZA® has been able to reach many more underserved TED patients than most had originally anticipated.

[7] https://www.fiercepharma.com/pharma/tepezza-sales-still-stagnant-amgen-has-plan-boost-newly-acquired-ted-drug

Case Studies

NURTEC ODT® Case Study (Runner-Up Drug of the Year)

Background: Migraine is an episodic disorder characterized by a severe headache and is considered the second leading cause of disability in the world with a prevalence of ~40M in the U.S. Overall, the migraine market is saturated with generic and branded products that are either approved for treatment or prevention of migraine. NURTEC ODT® was initially approved in 2020 for the treatment of migraine and expanded to the prevention of migraine in 2021, becoming the first therapy with the dual indication.

Results: NURTEC ODT® was able to surpass analyst expectations and achieve significant sales early in their launch, and within 6 months of launching, NURTEC ODT® achieved ~50% market share within oral CGRPs. As of 2022, NURTEC ODT® has been prescribed over 3.4M times worldwide and is anticipated to surpass $1B in sales by the end of 2023 with peak WW sales estimated to be >$3.5B by 2028. Additionally, in large part due to the success of NURTEC ODT®, Biohaven was acquired by Pfizer in 2022.

Commercial Learnings: Biohaven was able to capitalize on a **strong clinical profile through a digitally focused direct-to-consumer ad campaign and pre-launch market shaping.** NURTEC ODT® represents an example of a smaller company being able to have a successful launch despite launching into a market with significant competition from larger companies (e.g., Allergan and Eli Lilly). Ultimately, innovative and differentiated therapies, such as NURTEC ODT®, will be able to find success.

"NURTEC ODT® was able to surpass analyst expectations and achieve significant sales early in their launch, and within 6 months of launching, NURTEC ODT® achieved ~50% market share within oral CGRPs. Biohaven was able to capitalize on a strong clinical profile through a digitally focused direct-to-consumer ad campaign and pre-launch market shaping."

Case Studies

TRODELVY® Case Study (#3 Drug of the Year)

Background: Triple negative breast cancer (TNBC) is a highly severe, rapidly progressing solid tumor malignancy whose patients are negative across all key biomarkers: hormone receptors (HR) and human epidermal growth receptor 2 (HER). This market accounts for ~10-15% of all breast cancer cases and has long been characterized by poor patient response to chemotherapy and a dearth of targeted options. TRODELVY® was approved as the first antibody-drug conjugate, repackaging longstanding technology to generate a more targeted effect than traditional chemotherapy. Nearly tripling median progression-free survival (PFS) over chemotherapy, TRODELVY® offers a compelling clinical profile to patients who have already tried and failed another treatment for their metastatic disease.

Results: **TRODELVY®'s strong survival benefit over existing standard of care among an extremely high unmet need subset of breast cancer patients** propelled it to rapid commercial success. Despite launching in the middle of the initial wave of COVID-19 in April 2020, TRODELVY® quickly captured over 30% patient share in the 2L market and garnered over $120M in sales by the end of its first year. Efficacy is king in Oncology, and prescribers were quick to adopt this new regimen for its labeled population despite accompanying black box warnings.

Commercial Learnings: Within five months of TRODELVY® approval, Gilead made a hefty $21B investment to take over manufacturer Immunomedics for the right to market the product. Offering the commercial capabilities to realize the potential ~$3B peak sales that analysts expect for TRODELVY® by 2028, Gilead went all in on the TROP-2 ADC as a strategic play to establish its Oncology foothold. The bold move solidified Gilead's status as a key player in the space with a solid tumor anchor, on top of its existing presence in niche, relapsed/refractory (R/R) hematologic malignancies with prior CAR-T purchases. With a relatively straightforward mechanism and impressive efficacy for hard-to-treat patients, TRODELVY® figures to feature as an important treatment in the TNBC paradigm for the foreseeable future, particularly with additional indication expansions imminent (HR+/HER2-breast cancer, bladder cancer).

"TRODELVY's® strong survival benefit over existing standard of care among an extremely high unmet need subset of breast cancer patients propelled it to rapid commercial success. Within five months of TRODELVY® approval, Gilead made a hefty $21B investment to take over manufacturer Immunomedics for the right to market the product."

Case Studies

EVRYSDI® Case Study (#4 Drug of the Year)

Background: Spinal muscular atrophy (SMA) is a rare disease (~30K U.S. patients) that primarily manifests in infants or toddlers and is characterized by progressive muscle weakness, delayed motor skills and difficulty breathing. EVRYSDI® was approved in adult and pediatric patients as the third treatment and first oral systemic therapy in SMA behind SPINRAZA® (intrathecal injection) and ZOLGENSMA® (one-time infusion). In May 2022, EVRYSDI® was approved for a label expansion into patients under two months old.

Results: Driven by an initial bolus of high unmet need patients, oral dosing and a safe profile for patients with thrombocytopenia or kidney disease, **EVRYSDI® experienced rapid uptake, achieving >20% market share in the first 11 months and reaching >$1.0B in sales by the end of 2022.** Roche reports that EVRYSDI® is now the market leader for switches and naïve patient starts and is anticipated to achieve ~$2.8B in WW sales by 2028.

Commercial Learnings: As the third therapy to launch in SMA, EVRYSDI® greatly benefited from prior market shaping from competitors as robust patient identification programs were already in place. These programs helped create an initial bolus of patients who were not ideal candidates for SPINRAZA® or ZOLGENSMA®. EVRYSDI® was able to differentiate itself from competitors with a clear value proposition of convenience compared to intrathecal SPINRAZA®, ultimately leading to fast uptake and commercial success.

> “EVRYSDI® experienced rapid uptake, achieving >20% market share in the first 11 months and reaching >$1.0B in sales by the end of 2022. As the third therapy to launch in SMA, EVRYSDI® greatly benefited from prior market shaping from competitors as robust patient identification programs were already in place.”

Looking Ahead to 2021 Approvals

In 2021, there were a combined **59 novel drug and biological license application approvals, continuing an ongoing upward trend in approvals over the last 5 years.** Noteworthy approvals included full approval of the first mRNA COVID vaccine (COMIRNATY®), the first Kirsten rat sarcoma virus oncogene (KRAS) inhibitor for Oncology (LUMAKRAS®) and the first targeted therapy for Alzheimer's (ADUHELM®). New approvals span a wide array of therapeutic areas and over 60% of approvals received orphan drug designation. We look forward to profiling the innovations of 2021. Briefly, 17 of the novel products were approved in the Oncology therapeutic area, followed by 9 therapeutics launched in the Infectious Disease space and 8 in the Neurology space.

Appendix

The overall score of each drug made up of three weighted categories: commercial score, therapeutic score and R&D score. Each category includes several weighted metrics.

Commercial (40%): consists of 1) how well the product has performed first three years following launch (40%); 2) the latest sales expectations over the next four years (40%); 3) how well the product is doing compared to its original sales expectations over the first two years post-launch (20%).

Therapeutic (40%): consists of an internal Trinity survey sent to managers and leadership team in order to understand 1) how well each drug compares to prior SOC (60%); level of unmet need in indication (20%); and 3) the novelty of the drug based on its modality, technology and overall clinical profile (20%).

R&D (20%): consists of 1) total number of patients enrolled across all trials supporting regulatory approval, adjusted for relative trial cost by therapeutic area (50%); 2) total duration of clinical development from phase I to approval (50%).

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