TRINITY

WHITE PAPER

Trinity Annual Drug Index

Evaluating the Actual Commercial Performances of Novel Drugs Approved in 2019

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Introduction

This report, the fifth 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 2019, scoring each on its commercial performance, therapeutic value, and R&D investment (Table 1: Drug ranking – Ratings on a 1-5 scale).[1] 2019 saw 53 unique drug and biologic approvals, of which the majority were neurology (~23%) followed by oncology (~21%). 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.

2019 FDA Approvals

53

unique drug and biologic approvals

23%

of approvals were neurology

21%

of approvals were oncology

[1] Please see the appendix for the methodology

Key Highlights

1. Neurology Takes Center Stage in 2019

2019 saw a marked increase in the number of drugs approved within the neurology space, jumping to ~23% (12/53) new approvals in 2019 – up from ~11% (6/56) in 2017 and ~6% (4/65) 2018. Oncology approvals were down – with only ~21% (11/53) approvals in 2019 – vs. ~23% (13/56) in 2017 and ~25% (16/65) in 2018. This was the second time between 2016-19 that oncology was not the therapeutic area with the most product approvals. Neurology drugs approved in 2019 averaged ~$54 million and ~$117 million in years 1 and 2, respectively, compared to ~$24 million and ~$85 million for oncology drugs. **Neurology assets launched in 2019 also outpaced Oncology 2019 launches in 2021 net sales.** Approximately half of the launches in the neurology space were indicated for neuropsychiatric disorders including large indications such as migraine (REYVOW® – Eli Lilly, UBRELVY® – AbbVie), narcolepsy (WAKIX® – Harmony Biosciences), and depression (ZULRESSO® – Eisai). Only 25% (3/12) of drugs approved in 2019 were for rare indications including Duchenne muscular dystrophy (DMD) (VYONDYS 53® – Sarepta Therapeutics), Lambert-Eaton Myasthenic Syndrome (LEMS) (FIRDAPSE® – Catalyst Pharmaceuticals), and Spinal Muscular Atrophy (ZOLGENSMA® – Novartis). Two neurology drugs, UBRELVY® (AbbVie) and ZOLGENSMA® (Novartis), represent two of the top ten highest scoring drug launches.

2. Oncology Continues to Get More Targeted

Of the 11 drugs approved for Oncology indications, ~73% (8/11) were small molecule drugs (SM) while ~27% (3/11) were antibody drug conjugates (ADC). 50% (4/8) of the approved SM were mutant-targeted: ROZLYTREK® (Roche), BALVERSA® (Johnson & Johnson), PIQRAY® (Novartis). Only one ADC was mutant-targeted: ENHERTU® (AstraZeneca and Daiichi Sankyo). ~45% (5/11) therapies were first in class mechanistic targets, including the first PI3Ki (PIQRAY®), CD79b (POLIVY®), and Nectin-4 (PADCEV®).

While there were no novel immune-oncology therapies approved, the high volume of mutant targeted therapies, ADCs and novel drug targets reflects the general trend that successful agents in oncology are novel, targeted and can launch into multiple indications.

82% (9/11) were approved in large cancer types including breast cancer: ENHERTU® (AstraZeneca and Daiichi Sankyo), PIQRAY® (Novartis), prostate cancer: NUBEQA® (Bayer), and bladder cancer: BALVERSA® (Johnson & Johnson), PADCEV® (Seagen). Only ~18% (2/11) were approved in rare cancer types including osteosarcoma: TURALIO® (Daiichi Sankyo), and myelofibrosis: INREBIC® (Bristol Myers Squibb). Oncology drugs approved in 2017 and 2018 primarily focused on large cancer types too, but with a greater focus on Leukemia indications including acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), hairy cell leukemia (HCL). Other cancer types approved in 2017 and 2018 but not in 2019 include melanoma and colorectal cancer.

3. Companies that Launched their First Products Generally Struggled to Meet Forecast Expectations

~15% (8/53) of approved products in 2019 constituted a "first launch" for their respective companies. Of the "first launch" products, ~38% were approved for neurology indications including FIRDAPSE® (Catalyst Pharmaceuticals), WAKIX® (Harmony Biosciences), and ZULRESSO® (Sage Therapeutics), and ~25% were approved for oncology indications including XPOVIO® (Karyopharm Therapeutics) and BRUKINSA® (BeiGene). **Only one "first launch" product, OXBRYTA®, surpassed its forecast expectations, with the majority slightly underperforming (~33-67% of forecast expectations),** while ~33% of non-"first launch" products overperformed (>133% of forecast expectations). It's worth noting that none of the top ten highest scoring products in 2019 were "first launches" for their respective companies.

4. Almost One Third of Drugs that Launched in Indications without Prior Approvals Exceeded Forecast Expectations

~13% (7/53) of approved products in 2019 constituted "first in indication" with ~29% approved for neurology indications (FIRDAPSE® – Catalyst Pharmaceuticals, VYONDYS 53® – Sarepta Therapeutics) and ~29% approved for oncology indications (XPOVIO® – Karyopharm Therapeutics, TURALIO® – Daiichi Sankyo). "First in indication" products tended to be indicated for smaller indications such as LEMS (FIRDAPSE® – Catalyst Pharmaceuticals), transthyretin amyloid cardiomyopathy (ATTR-CM) (VYNDAQEL® - Pfizer), and Duchenne muscular dystrophy (DMD) (VYONDYS 53® – Sarepta Therapeutics). **~29% of the "first in indication" products surpassed forecast expectations, ranging from ~133-300% over forecast expectations, though the majority slightly underperformed, reaching ~67% of forecast expectations.** Interestingly, no "first in indication" products significantly underperformed (<33% of forecast expectations). The spread of non-"first in indication" product performance relative to forecast expectations was more evenly distributed across the ranges, with ~20% significantly underperforming. **Of the top ten highest performing drugs in 2019, VYNDAQEL® was the only asset to be a "first in indication" product.**

23% of **2019** approvals were within the **neurology space**

Of the **11 drugs approved for oncology indications**, 73% (8 of 11) were small molecule drugs, while 27% (3 of 11) were antibody drug conjugates.

Only **1of 8** first launch companies surpassed its forecast expectations.

29% of the "first in indication" products surpassed forecast expectations

Drug Ranking

The overall and component scores for each drug are shown in Table 1 (see page 2). 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 tenured 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	2019 Indication Approval[1]	FDA Approval Date	Reported Revenue in 2019 ($Million)	Reported Revenue in 2020 ($Million)	Component Scores			Overall Score
						Therapeutic Score	Commercial Score	R&D Score	
TRIKAFTA® (Vertex Pharmaceuticals)	Pulmonology	Cystic Fibrosis	10/21/2019	$420.1	$3,863.8	4.8	4.8	2.0	4.2
VYNDAQEL® (Pfizer)	Cardiology	TTR Cardiomyopathy	5/3/2019	$191.0	$613.0	5.0	4.0	3.0	4.2
SKYRIZI® (AbbVie)	Dermatology	Psoriatic Arthritis	4/23/2019	$311.0	$1,385.0	4.4	4.4	2.5	4.0
ZOLGENSMA® (Novartis)	Neurology	Spinal Muscular Atrophy	5/24/2019	$361.0	$459.0	4.4	3.0	4.5	3.9
PADCEV® (Seagen)	Oncology	Bladder cancer	12/18/2019	$0.2	$222.4	4.4	3.8	2.5	3.8
ADAKVEO® (Novartis)	Hematology	Sickle Cell Disease	11/15/2019	$0.0	$105.0	4.2	2.4	5.0	3.6
UBRELVY® (AbbVie)	Neurology	Migraine	12/23/2019	$0.0	$125.0	3.8	3.8	3.0	3.6
GIVLAARI® (Alnylam Pharmaceuticals)	Hepatology	Porphyria	11/20/2019	$0.2	$55.1	5.0	1.8	4.5	3.6
RINVOQ® (AbbVie)	Rheumatology	Rheumatoid Arthritis	8/16/2019	$47.0	$653.0	3.6	4.4	1.5	3.5
ENHERTU® (AstraZeneca & Daiichi Sankyo)	Oncology	Breast cancer	12/20/2019	$18.4	$40.6	4.0	2.8	3.5	3.4
OXBRYTA® (Global Blood Therapeutics[2])	Hematology	Sickle Cell Disease	11/25/2019	$2.1	$123.8	4.2	2.6	3.5	3.4
WAKIX® (Harmony Biosciences)	Neurology	Narcolepsy	8/14/2019	$6.0	$159.7	3.6	2.6	4.0	3.3
EVENITY® (Amgen)	Endocrinology	Osteoporosis	4/9/2019	$42.0	$191.0	3.8	3.4	1.5	3.2
REBLOZYL® (Bristol Myers Squibb)	Hematology	Thalassemia	11/8/2019	$12.4	$51.8	4.0	2.4	3.0	3.2
PIQRAY® (Novartis)	Oncology	Breast cancer	5/24/2019	$116.0	$320.0	4.0	2.8	2.0	3.1
CABLIVI® (Sanofi)	Hematology	Thrombotic Thrombocytopenic Purpur	2/6/2019	$38.1	$82.2	4.4	1.4	4.0	3.1
XCOPRI® (SK)	Neurology	Epilepsy	11/21/2019	$0.0	$9.6	4.0	1.6	4.0	3.0
VYONDYS 53® (Sarepta Therapeutics)	Neurology	Duchenne Muscular Dystrophy	12/12/2019	$0.0	$42.8	4.2	1.4	4.0	3.0
FIRDAPSE® (Catalyst Pharmaceuticals)	Neurology	Lambert-Eaton Myasthenic Syndrome	5/6/2019	$102.3	$118.7	3.6	2.2	3.5	3.0
BALVERSA® (Johnson & Johnson)	Oncology	Bladder cancer	4/12/2019	$20.0	$6.7	4.2	1.6	3.5	3.0

[1] Certain products in multi-year analysis have been approved for multiple indications since initial approval in 2019. 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 2019 products: **ACCRUFER®, XEMBIFY®, JYNNEOS®, EGATEN®, SCENESSE®, TENAPANOR®, RECARDBIRO®, AKLIEF®, ERVEBO® and DENGVAXIA®**

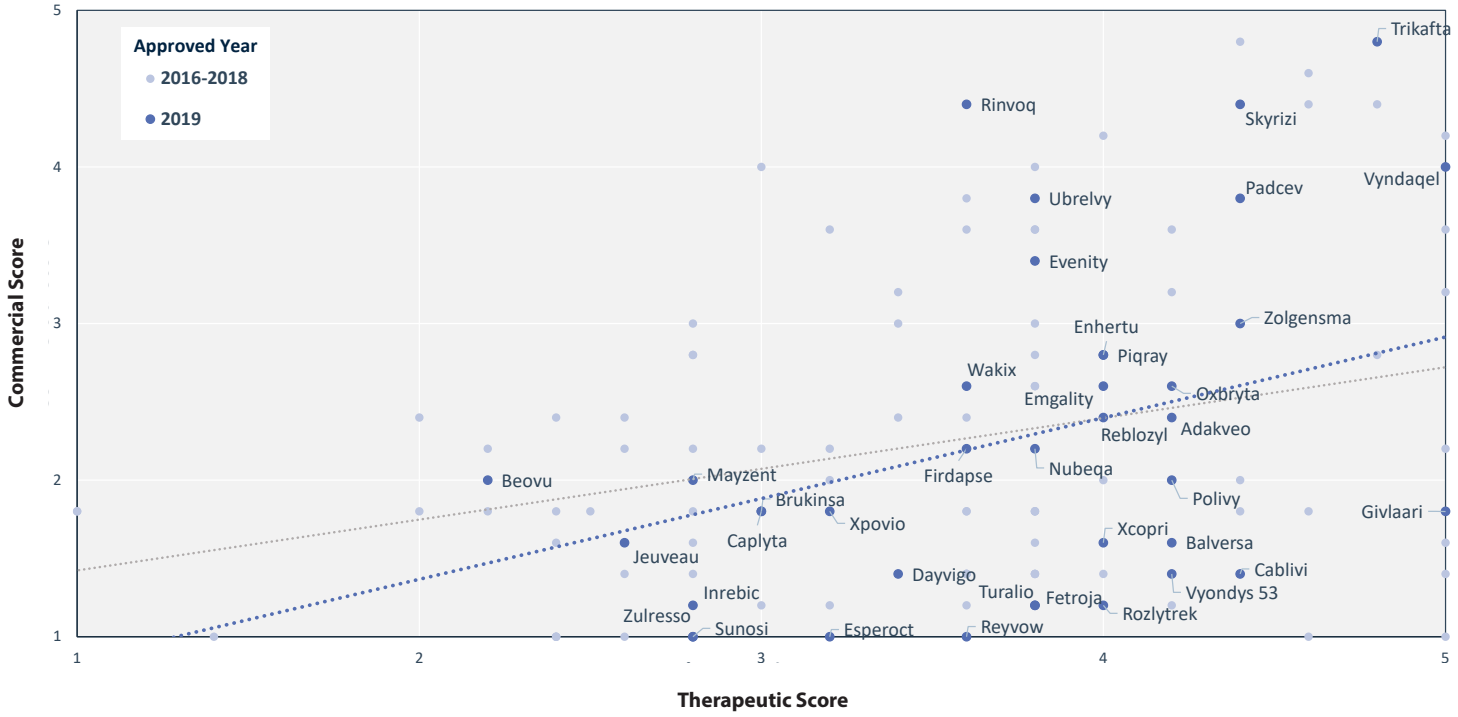
[2] Global Blood Therapeutics is now owned by Pfizer.

Brand Name (Company)	Therapeutic Area Approval	2019 Indication Approval	FDA Approval Date	Reported Revenue in 2019 ($Million)	Reported Revenue in 2020 ($Million)	Component Scores			Overall Score
						Therapeutic Score	Commercial Score	R&D Score	
ROZLYTREK® (Roche)	Oncology	NSCLC	8/15/2019	$7.0	$25.6	4.0	1.2	4.5	3.0
POLIVY® (Roche)	Oncology	Non-Hodgkin Lymphoma	6/10/2019	$51.3	$110.9	4.2	2.0	2.5	3.0
NUBEQA® (Bayer)	Oncology	Prostate Cancer	7/30/2019	$0.9	$55.7	3.8	2.2	2.5	2.9
EMGALITY® (Eli Lilly)	Neurology	Migraine	6/4/2019	$154.9	$325.8	4.0	2.6	1.0	2.8
FETROJA® (Novartis)	infectious disease	Urinary tract infections	11/14/2019	$2.2	$16.0	3.8	1.2	3.5	2.7
XPOVIO® (Karyopharm Therapeutics)	Oncology	Multiple myeloma	7/3/2019	$30.5	$76.2	3.2	1.8	3.0	2.6
TURALIO® (Daiichi Sankyo)	Oncology	Osteosarcoma	8/2/2019	$10.3	$9.4	3.8	1.2	3.0	2.6
BRUKINSA® (BeiGene)	Oncology	Non-Hodgkin lymphoma	11/14/2019	$0.0	$11.9	3.0	1.8	3.0	2.5
ESPEROCT® (Novo Nordisk)	hematology	Hemophilia A	2/19/2019	$0.0	$8.4	3.2	1.0	4.0	2.5
JEUVEAU® (Evolus)	Dermatology	Facial Wrinkles	2/1/2019	$34.2	$55.8	2.6	1.6	4.0	2.5
REYVOW® (Eli Lilly)	Neurology	Migraine	10/11/2019	$0.0	$12.4	3.6	1.0	3.0	2.4
DAYVIGO® (Eisai)	Neurology	Insomnia	12/20/2019	$0.0	$10.4	3.4	1.4	2.0	2.3
CAPLYTA® (Intra-Cellular Therapies)	Psychiatry	Bipolar disorder	12/20/2019	$0.0	$0.0	3.0	1.8	2.0	2.3
MAYZENT® (Novartis)	Neurology	Secondary-Progressive MS	3/26/2019	$16.8	$109.6	2.8	2.0	2.0	2.3
SUNOSI® (Jazz Pharmaceuticals[3])	Neurology	Obstructive Sleep Apnea	3/20/2019	$3.0	$22.7	2.8	1.0	4.0	2.3
ZULRESSO® (SAGE Therapeutics)	Neurology	Depression	3/19/2019	$4.0	$6.7	2.8	1.0	3.5	2.2
INREBIC® (Bristol Myers Squibb)	Oncology	Myelofibrosis	8/16/2019	$5.0	$55.0	2.8	1.2	2.5	2.1
BEOVU® (Novartis)	Ophthalmology	Wet Age-Related Macular Degeneration	10/7/2019	$35.0	$190.0	2.2	2.0	1.0	1.9

[3] GW Pharmaceuticals is now owned by Jazz Pharmaceuticals.

Figure 1. Comparison of therapeutic and commercial scores for drugs approved by the FDA, 2019

The line below is the linear regression of commercial score on therapeutics score for drugs approved by the FDA and included across all the drugs approved in 2019, relative to the rest of the Drug Indices from 2016-2018



Key Themes

Commercial Performance Showing Greater Variability

Products approved in 2019 showed greater variability in the annual commercial performance as a function of therapeutic value when compared to results from 2016-2018. As a result, there were more products at the extremes, especially ones that performed poorly from both a therapeutic and commercial perspective. Products launched in 2019 that did perform poorly commercially had unfavorable therapeutic profiles; assets with favorable therapeutic profiles tended to see greater commercial success. **Despite COVID-19 being a major headwind for products approved in 2019, there was not a statistical difference in the average commercial performance relative to 2017 and 2018.** Furthermore, we did not observe a meaningful change in the proportion of drugs that failed to meet or exceed forecast expectations over the first two years post-launch. We hypothesize that COVID had a limited impact on the products that launched in 2019 because the respective companies had time to establish commercialization plans before the industry felt COVID's effects. Having the opportunity to solidify commercialization plans likely enabled companies to focus their time and efforts on transitioning to remote work and leverage telemedicine to ensure patients would be able to continue receiving therapies. **COVID's impact is likely to be felt more directly by products launched in 2020 and 2021.**

COVID's impact is likely to be felt more directly by products launched in 2020 and 2021.

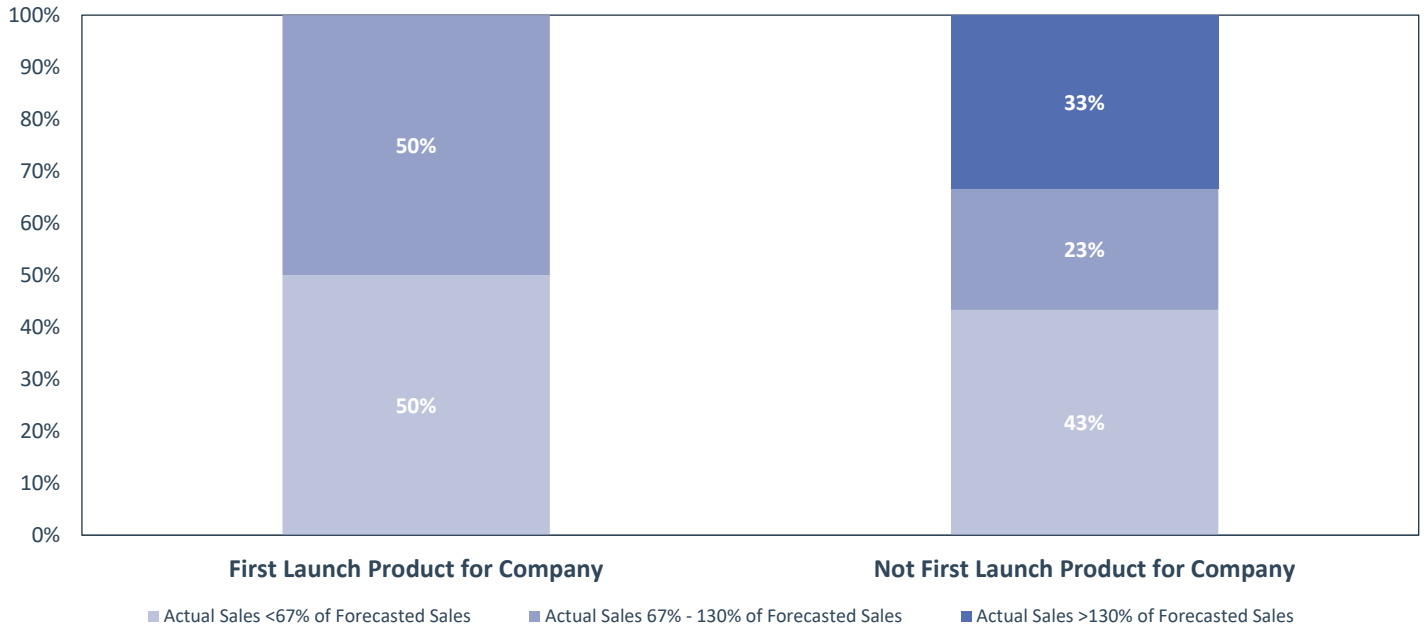
Struggling First Launch Companies

Products in 2019 that constituted a "first launch" for their respective companies performed poorly overall, with only ~50% near commercial expectations over the first two years post-launch. ~33% of first launch companies failed to meet commercial performance expectations altogether, and none significantly exceeded expectations. Meanwhile, ~33% of products that were not a "first launch" product exceeded commercial expectations, underscoring the difficulty in ensuring commercial success for companies launching their first product. **Delivering a successful launch requires detailed planning including internal organization (strategic imperatives for product, cross-functional engagement), marketing (disease state education, brand strategy), salesforce organization (structure, sizing, alignment), value and access (private and government contracting, payer CRM), and patient services (price communication plan, supporting patient services), etc., prior to launch.** The team urges first launch companies to begin thoughtful planning as early as possible in order to have a smoother launch process.

"Delivering a successful launch requires detailed planning including internal organization (strategic imperatives for product, cross-functional engagement), marketing (disease state education, brand strategy), salesforce organization (structure, sizing, alignment), value and access (private and government contracting, payer CRM), and patient services (price communication plan, supporting patient services), etc., prior to launch."

Figure 2. Comparison of commercial performance by product type in 2019: "first launch" product for company vs not first launch product 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?



Larger Competitive Markets with Large Companies Performed Strongest

Looking at the top-rated products that launched in 2019, the majority (~70%) were launched by large companies (AbbVie, UCB, Vertex) in major established markets (psoriasis, rheumatoid arthritis, osteoporosis, etc.) with relatively high competition. Comparatively, products that fell below the trend line and performed poorly were typically smaller companies in less prevalent indications with an overall lower market potential. **Overcoming a smaller market potential based on prevalence can be extremely difficult, but not impossible, as evidenced by highly innovative products like ZOLGENSMA® or VYNDAQEL®, which were able to overcome relatively small market potential and deliver commercially in 2019.** Differentiation and innovation are all the more important to achieve success for companies launching with only one indication or into rare / small markets given the lower potential patient volume compared to assets that can string together successful launches.

Case Study

TRIKAFTA® (Drug of the Year)

Background: Cystic fibrosis (CF) treatment had been dominated by symptomatic therapies until the 2012 approval of KALYDECO®, a cystic fibrosis transmembrane conductance regulator (CFTR) modulator and the first treatment approved to address the root cause of this debilitating disease. However, at launch, only ~4% of CF patients were eligible for KALYDECO®. Since this initial approval, Vertex Pharmaceuticals has expanded its CF franchise through a number of KALYDECO® indication expansions and a variety of combination therapy approvals built on a KALYDECO® backbone. Highlights include ORKAMBI®, SYMDEKO® and most recently, TRIKAFTA®, which combines agents from all three previously approved treatments and has the broadest set of addressable patients yet (~90%). Although TRIKAFTA® is a relatively new product, performance to date indicates an impressive launch and subsequent uptake, riding superior efficacy data and broader label relative to its CFTR modulator predecessors. Leveraging a strong infrastructure and expertise in the indication, Vertex offers robust patient support services including copay support, first drug shipment coordination, educational resources, and much more, that have paved the way for TRIKAFTA®'s success.

Results: **Garnering over $420 million in sales over its first 10 weeks on the market,** TRIKAFTA® has proven a boon for Boston-based Vertex and made headlines as the second biggest pharmaceutical launch (behind Gilead's HARVONI®) in the five-year period from 2015-2020. Patients quickly switched off previously approved CFTR modulators in favor of the newly approved TRIKAFTA®, accelerating uptake as nearly all patients were eligible.

Commercial Learnings: Vertex has monopolized branded treatment of cystic fibrosis over the past decade, and TRIKAFTA® is the crown jewel. Rare disease commercialization can be hampered by a number of factors (e.g., challenges with identifying eligible patients, gaining the trust of the patient community, and in some cases supplanting existing competitors); however, TRIKAFTA® was able to avoid many of these hurdles given Vertex's longstanding leadership in CF and strong patients services organization deeply integrated in the patient community. Treating a very well-identified patient population with minimal competition, entering an indication with years of existing manufacturer presence, and boasting a transformational efficacy profile, TRIKAFTA® has propelled itself to ultra-blockbuster status, raking in ~$5.7 billion worldwide in its third year on the market.

> "Garnering over $420 million in sales over its first 10 weeks on the market, TRIKAFTA® has proven a boon."

Case Study

VYNDAQEL® (Runner-Up Drug of the Year)

Background: Prior to VYNDAQEL® approval in 2019, there was no treatment available for transthyretin cardiac amyloidosis (ATTR-CM), a rare, progressive disease eventually leading to heart failure that affects an estimated ~100K patients in the U.S. While VYNDAQEL® was able to demonstrate impressive efficacy in the clinic, including significantly reduced all-cause mortality and cardiovascular-related hospitalizations compared to placebo, Pfizer faced an uphill battle to get the drug to patients, given ATTR-CM's dismal ~1-2% diagnosis rate at launch. Of note, competitors ONPATTRO® and TEGSEDI® were approved in 2018 for the treatment of transthyretin amyloid polyneuropathy (ATTR-PN), and while some patients do present with mixed phenotypes (CM and PN), these agents have not been approved for patients with ATTR-CM.

Results: By the end of its **second full quarter on the market, VYNDAQEL® reached nearly $200 million in U.S. sales.** Given the high unmet need and lack of available alternatives for ATTR-CM patients, diagnosis rate will be the key driver of VYNDAQEL® opportunity in this indication. Since approval, Pfizer has expanded disease awareness among treating physicians by developing a red-flag symptom checklist and pushing for broader adoption of non-invasive cardiac imaging technology known as scintigraphy. By the end of 2020, ATTR-CM diagnosis rate had reached 21%, and Pfizer's VYNDAQEL® was well on its way to blockbuster status, garnering over ~$600 million in its second year on the market.

Commercial Learnings: Launching the first product in a difficult to diagnose orphan indication, Pfizer carried much of the weight of shaping the ATTR-CM market. However, signs are positive so far with Pfizer's patient identification campaigns driving consistent year over year growth in diagnosis rates. In addition to ATTR-CM, Pfizer has kept its eyes on ATTR-PN, for which VYNDAQEL® has been marketed in the EU for over a decade but rejected by the FDA in 2012 due to lack of data. A potential expansion into this adjacent (and comparatively smaller) indication could provide additional upside to an already strong outlook and spell trouble for competitors TEGSEDI® and ONPATTRO®, whose price tags are currently double that of VYNDAQEL®.

> "By the end of its second full quarter on the market, VYNDAQEL® reached nearly $200 million in U.S. sales."

Case Study

SKYRIZI® (#3 Drug of the Year)

Background: Historically, treatment of moderate-severe psoriasis has been dominated by anti-TNFs such as HUMIRA® due to long term safety data, strong efficacy, and favorable contracting. Recently, the market has shifted toward next generation therapies (e.g., IL-17s and IL-23s) due to superior efficacy and safety profiles vs. anti-TNFs. SKYRIZI®, AbbVie's successor to HUMIRA®, entered as a later agent relative to other next generation therapies into a crowded and heavily contracted market, but has shown relatively strong efficacy in both short-term and long-term response rate, and has favorable dosing (Q12W) compared to most competitive ILs approved for psoriasis (only STELARA® is Q12W), while maintaining a clean safety profile. AbbVie was able to time the launch of SKYRIZI® to coincide with HUMIRA®'s loss of exclusivity in order maximize the commercial potential and limit cannibalization.

Results: **SKYRIZI® currently ranks as one of the top products ever analyzed in the drug index with strong therapeutic and commercial scores.** Initially, SKYRIZI® had rapid uptake capturing a significant amount of market share and revenue within ~1.5 years after launch due to a strong product profile and robust commercialization efforts. AbbVie has been able to expand SKYRIZI® into psoriatic arthritis and Crohn's Disease, with approvals in both indications earlier this year and to date, **SKYRIZI® is anticipated to achieve > $4 billion in WW sales.**

Commercial Learnings: AbbVie benefitted from prior expertise and massive presence in psoriasis due to HUMIRA®'s success, which led to a successful launch of SKYRIZI®. However, SKYRIZI® was able to achieve continued success through a superior profile and expansion into other indications (Psoriatic arthritis and Crohn's Disease). Strategic staggering of indications and a strong clinical profile kept SKYRIZI® top of mind for physicians, leading to high utilization.

> "SKYRIZI® currently ranks as one of the top products ever analyzed in the drug index with strong therapeutic and commercial scores. SKYRIZI® is anticipated to achieve > $4 billion in WW sales."

Case Study

ZOLGENSMA® (#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. ZOLGENSMA® was approved in 0–1-year-old infants as the first gene therapy and second treatment for SMA, offering a potentially curative (at least for a number of years) treatment with one-time dosing. However, ZOLGENSMA® did receive coverage delays due to manipulation of data in preclinical trials and a launch price of ~$2.1million.

Results: Following the launch, ZOLGENSMA® had a rapid initial uptake peaking in ~1 year post launch due to improved dosing and a potentially curative profile. ZOLGENSMA® particularly dominated in 0–1-year-old patients, because doctors and families were faced with a "use or lose it" situation, where they needed to give infants ZOLGENSMA® or never be allowed to take it. However, in the subsequent quarters after the first year, ZOLGENSMA® experienced a drop off in sales due to a bolus of patients receiving the one-time treatment. Nonetheless, **Novartis was able to maintain consistent YoY revenue by identifying patients via newborn screening, which currently covers ~85% of U.S. live births.** As of Q3'22, Novartis stated that ZOLGENSMA® sales are now predominantly driven by the incident patient population, of which ZOLGENSMA® commands 80% market share (according to analyst estimates). Additionally, **Novartis has provided robust patient support based on a HUB model which supports patients along the treatment journey, ensuring access, affordability, and logistical ease.**

Commercial Learnings: Innovative therapies, particularly **one-time treatments with high price tags, can face significant commercial challenges.** The ZOLGENSMA® launch likely benefited greatly from the commercial experience Novartis garnered through the launch of KYMRIAH® – while there are significant differences in the therapies, target patient populations, etc., the tangible and intangible experience of relationships with treatment centers, operational learnings, and general launch experience likely carried over from the cell therapy to the gene therapy launch. Additionally, as evidenced by a slight dip in year 2 sales, manufacturers developing one-time treatments need to be proactive in identifying patients, as there is no guarantee for year-over-year sales like other therapies.

> "Novartis was able to maintain consistent YoY revenue by identifying patients via newborn screening, which currently covers ~85% of U.S. live births. Novartis has provided robust patient support based on a HUB model which supports patients along the treatment journey, ensuring access, affordability, and logistical ease."

Looking Ahead

The 2019 approval landscape featured a number of highlights, including further validation of gene therapy technology, a glimpse into the future of big pharma Immunology and Inflammation (I&I) leadership, and a particularly strong neurology focus. ZOLGENSMA® marked the most successful gene therapy launch to date, while a string of recent gene therapy approvals, including ZYNTEGLO® (Beta-Thalassemia), SKYSONA® (Cerebral Adrenoleukodystrophy), and HEMGENIX® (Hemophilia B), look to build on this momentum and extend the applicability of gene therapy to additional orphan indications. SKYRIZI® set off the first wave of large pharma follow-ups to compensate for impending patent cliffs faced by existing blockbuster therapies in large dermatologic/rheumatologic indications, and ongoing development across key mechanisms (e.g. interleukins, JAK/TYKs, etc.) will determine the future of treatment in key I&I indications in the shadow of HUMIRA®. When it comes to 2019's comparatively strong batch of neurology approvals, it remains to be seen whether this represents a notable shift in pharmaceutical development focus or a one-year aberration from the mean. Future drug indices will be needed to evaluate how these trends and others evolve in the coming years.

Looking ahead to 2020, there were a combined 59 novel drug and biological license application approvals. New approvals span a wide array of therapeutic areas, and over half of approvals received orphan drug designation. We look forward to profiling the innovations of 2020 and understanding the impact of the COVID-19 pandemic on drug launches, relative to analyses in pre-pandemic years. **At a glance, 18 of the novel products were approved in the oncology therapeutic area, followed by 8 therapeutics launched in the CNS 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 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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Trinity is a trusted strategic commercialization partner, providing evidence-based solutions for the life sciences. With 25 years of experience, Trinity is revolutionizing the commercial model by providing exceptional levels of service, powerful tools and data-driven insights. Trinity's range of products and solutions includes industry-leading benchmarking solutions, powered by TGaS Advisors. To learn more about how Trinity is elevating life sciences and driving evidence to action, visit trinitylifesciences.com.

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