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Trinity Annual Drug Index

Evaluating the Commercial Performance and Impact of Novel Drugs Approved in 2021

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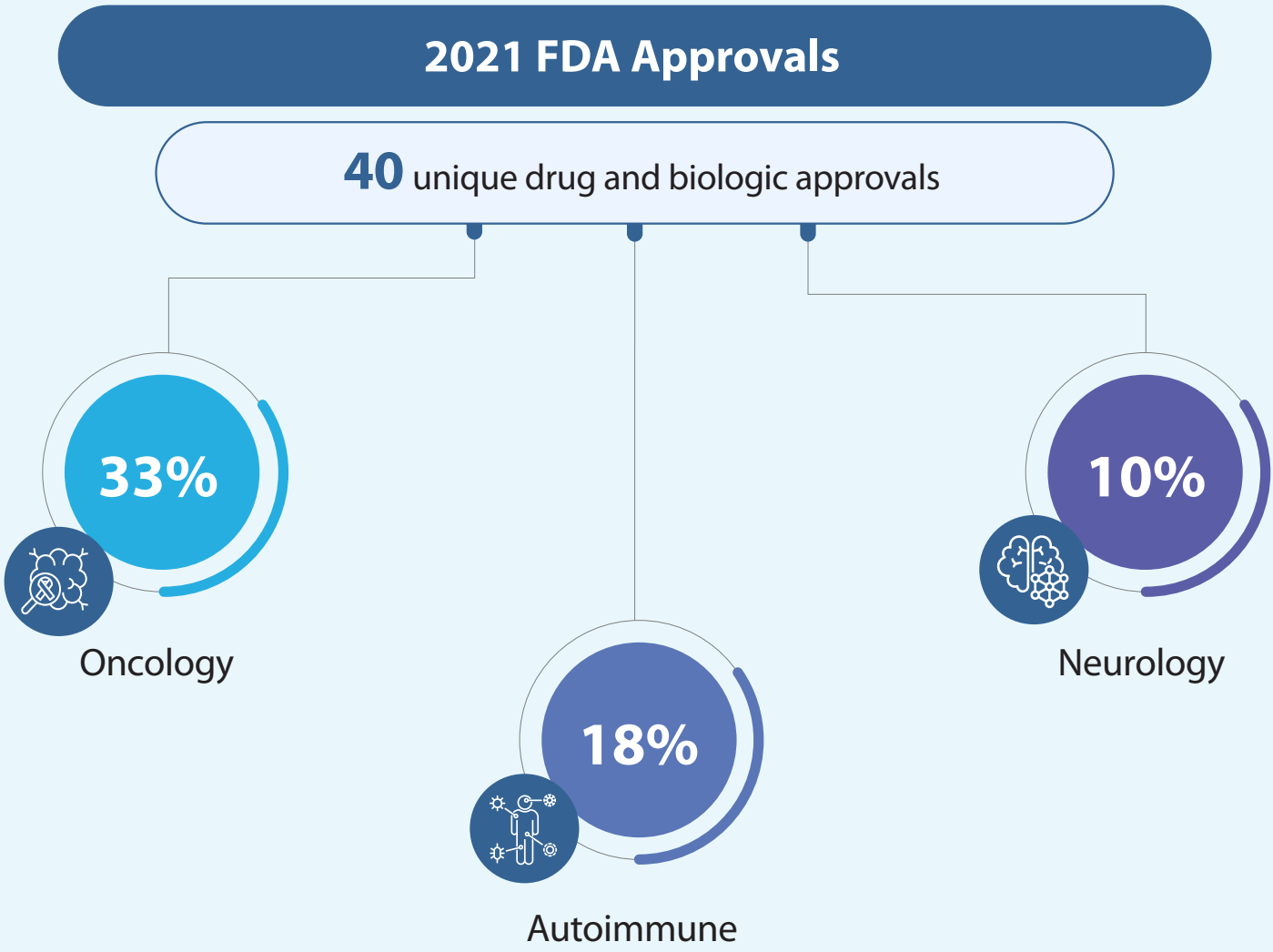
Introduction

This report, the seventh 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 2021, scoring each on its commercial performance, therapeutic value and R&D investment (Table 1: Drug ranking – Ratings on a 1–5 scale, see page 5). 2021 saw 40 unique drug and biologic approvals, of which ~33% (13/40) were Oncology, followed by ~18% (7/40) being Autoimmune and 10% (4/40) being Neurology. In this report we describe the notable themes and trends within the industry and take a deeper look at a few products with outstanding performance. Though the impact of the COVID-19 pandemic was primarily felt in 2020, 2021 fared worse than 2020 and sustained an ongoing decline in the relationship between a product's therapeutic value and its commercial output.



Key Highlights

1. 2021 Drug Launches Showed Poorer Commercial Performance Relative to Therapeutic Score

In 2021, drugs with strong clinical value did not achieve the same level of commercial success as seen in past years, demonstrated by the weaker relationship between commercial and therapeutic scores (see Figure 1 on page 7). This may be a result of market maturation, where new drugs face greater challenges in penetrating established markets that already have existing therapies. Consequently, the threshold for surpassing the current standard of care has become higher.

Even the best drugs of 2021 did not perform relative to their therapeutic value. This trend is reflected in their sales to date: The top 5 highest sales drugs launched in 2020 (TEPEZZA®, NURTEC®, EVRYSDI®, TRODELVY®, TUKYSA®) achieved $7.3B in Y1-Y3 cumulative U.S. revenue while the top 5 drugs launched in 2021 (VYVGART®, CABENUVA®, ABECMA®, RYLAZE®, TEZPIRE®) achieved only $4.9B.

2. First-Launch Companies Had More Success in 2021, But Continued to Underperform on Average

While, on average, first-launch companies in 2021 were less likely to overperform forecasts compared to companies with prior launches, the first-launch drugs that did overperform did so substantially.[1] In fact, a greater proportion of drugs from first-launch companies (33%, 3/9) achieved 3x forecasted sales (Y2-Y3) compared to only ~16% from companies with prior launches. This outperformance was driven by FOTIVDA® (AVEO Oncology), REZUROCK® (Kadmon), and VYVGART® (argenx), all of which were the first launches for their manufacturers at the time of launch. However, despite the outperformance of these select products, first-launch companies were also more likely to underperform forecast estimates, with ~67% of first-launch drugs underperforming. This polarity in the performance – either significant outperformance or significant underperformance – highlights the "make-or-break" nature of the first drug launch for these companies.

While no drugs from first-launch companies in 2020 exceeded forecast expectations (see Figure 2 on page 7), 2021 drug launches showed a clear signal of success for first-launch companies, especially in orphan and ultra-orphan indications. This trend suggests that first-launch companies are becoming more successful at and/or are more capable in launching potential blockbuster drugs.

[1] See Moving the Needle: Lessons from the 2023 Launch Class white paper for additional insight on the performance of first-launch companies from 2020-2023: https://trinitylifesciences.com/white-paper/moving-the-needle-lessons-from-the-2023-launch-class/

3. While Oncology Continues to Lead with the Most Approvals, Autoimmune Diseases Emerge as a Top Therapeutic Area, Surpassing Neurology

Of 2021 drug launches, oncology remained the most prevalent therapeutic area and continued to grow: oncology drugs represented ~33% (13/40) of approvals in 2021, up from ~29% (17/58) in 2020 and ~23% (12/43) in 2019. Of the 13 oncology drugs approved in 2021, 7 were small molecules, 4 were monoclonal antibodies, and 2 were CAR-T cell therapies.

In 2021, launch trends reflect a shift in the focus of the pharma industry towards autoimmune conditions, overtaking neurology as the second most common therapeutic area. Autoimmune drugs represented ~18% (7/40) of approvals in 2021, which is a relative increase from the last three years (autoimmune represented ~6-10% of approvals from 2018-2020).[2] Conversely, neurology drugs only represented 10% (4/40) of approvals in 2021, down from ~16% (9/58) in 2020.

4. Orphan Markets Remained a Bright Spot, While Ultra-Orphan Markets Continued to Underperform

Orphan drugs launched in 2021 greatly outperformed forecasts, including NEXVIAZME® (Sanofi), REZUROCK® (Kadmon[3]), RYLAZE® (Jazz Pharmaceuticals), and VYVGART® (argenx). However, ultra-orphan drugs (diseases with 5,000 or fewer prevalent U.S. patients) were more likely to underperform forecasts relative to the average drug launched in 2019. Drugs launched in large or primary care markets also underperformed forecast estimates relative to the average drug, likely due to the inordinate impact of COVID-19 pandemic on these markets.

[2] Classification of autoimmune overlaps with classification of other therapuetic areas (e.g., SLE is classified as both as an autoimmune and rhuematology condition, gMG is classified as both as a autoimmune and neurology condition)

[3] Later acquired by Sanofi

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)[4]

Brand Name (Company)	Therapeutic Area Approval	2021 Indication Approval[4]	FDA Approval Date	Reported Revenue in 2021 ($M)	Reported Revenue in 2022 ($M)	Component Scores			Overall Score
						Therapeutic Score	Commercial Score	R&D Score	
VYVGART® (argenx)	Neurology	Myasthenia gravis	12/17/2021	$0	$378	4.0	3.8	4.0	3.9
CABENUVA® (GSK)	Infectious Disease	HIV treatment	1/21/2021	$44	$368	4.8	3.0	3.0	3.7
LUMAKRAS® (Amgen)	Oncology	Non-small cell lung cancer (NSCLC)	5/28/2021	$82	$222	4.4	2.8	4.0	3.7
REZUROCK® (Kadmon)	Oncology	Graft vs host disease (GvHD)	7/16/2021	$26	$220	4.2	2.6	3.5	3.4
WELIREG® (Merck & Co)	Metabolic	Von Hippel-Lindau (VHL) disease	8/13/2021	$13	$123	4.8	2.0	3.5	3.4
ABECMA® (Bristol Myers Squibb)	Oncology	Multiple myeloma	3/26/2021	$158	$297	4.4	2.8	2.0	3.3
RYLAZE® (Jazz Pharmaceuticals)	Oncology	Leukaemia, acute lymphocytic (ALL)	6/30/2021	$86	$282	3.2	2.6	4.5	3.2
AMONDYS 45® (Sarepta Therapeutics)	Neurology	Duchenne muscular dystrophy	2/25/2021	$69	$215	4.0	2.4	3.0	3.2
LUPKYNIS® (Aurinia Pharmaceuticals)	Rheumatology	Systemic lupus erythematosus (SLE)	1/22/2021	$45	$103	4.0	2.4	3.0	3.2
BYLVAY® (Ipsen)	Gastrointestinal	Cholestasis	7/20/2021	$0	$0	4.6	1.2	4.0	3.1
LIVMARLI® (Mirum Pharmaceuticals)	Gastrointestinal	General liver disorders	9/29/2021	$3	$68	4.6	1.6	3.0	3.1
TAVNEOS® (ChemoCentryx)	Rheumatology	Vasculitis	10/07/2021	$1	$68	4.0	1.6	4.0	3.0
TEZSPIRE® (Amgen)	Pulmonology	Asthma	12/17/2021	$0	$170	4.0	3.0	1.0	3.0
NEXVIAZYME® (Sanofi)	Metabolic	Pompe's disease	08/06/2021	$17	$169	3.8	2.2	3.0	3.0
VOXZOGO® (BioMarin Pharmaceutical)	Endocrine	Achondroplasia	11/19/2021	$0	$64	4.8	1.6	2.0	3.0
BREYANZI® (Bristol Myers Squibb)	Oncology	Non-Hodgkin lymphoma (NHL)	02/05/2021	$84	$151	4.0	2.6	1.5	2.9
QULIPTA® (AbbVie)	Neurology	Migraine	9/28/2021	$0	$158	3.8	2.6	1.5	2.9
SKYTROFA® (Ascendis Pharma)	Endocrine	Short stature in children	8/25/2021	$1	$38	3.6	1.6	3.5	2.8

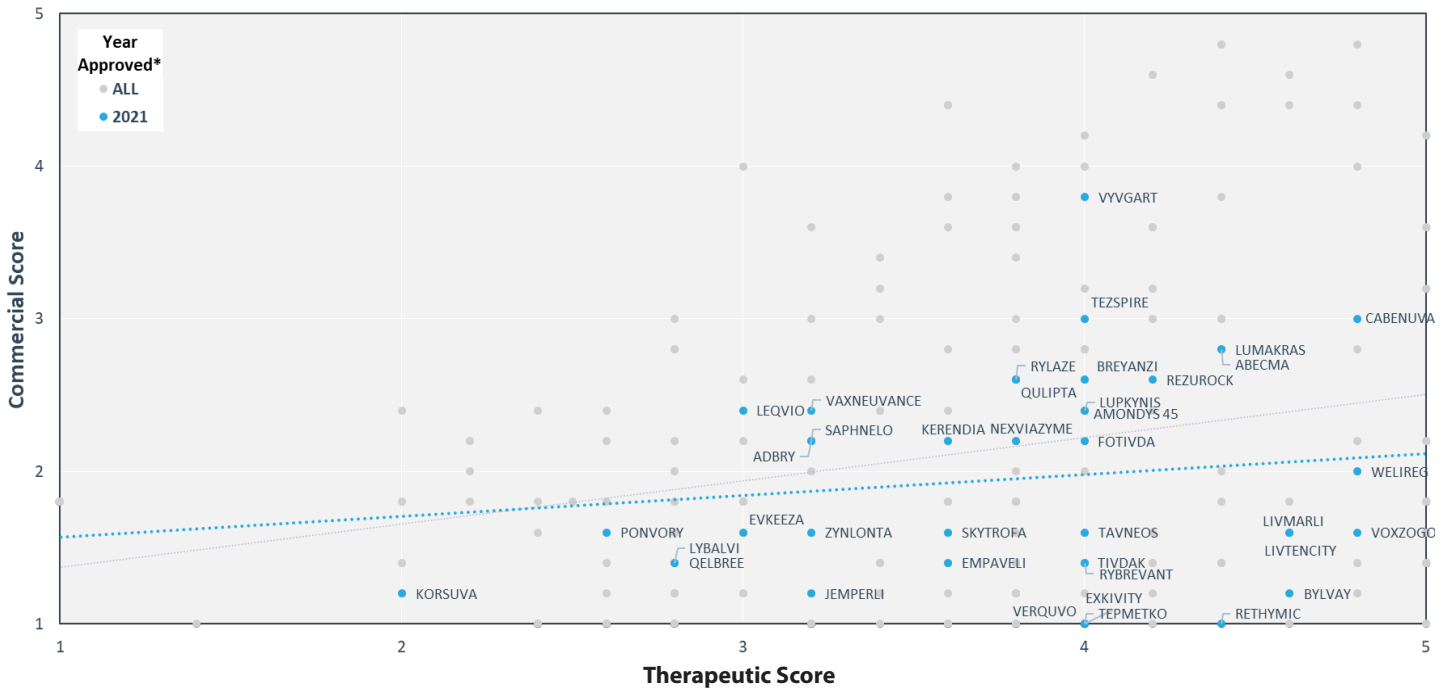
[4] Certain products in multi-year analysis have been approved for multiple indications since initial approval in 2021. As such, we have indicated the first indication approvals. Certain products were also omitted from the analysis due to limited financial data. Please note that this applies to the following 2021 products: **BESREMI®, FEXINIDAZOLE®, NULIBRY®, PREHEVBRIO®, PREVNAR 20®, RYPLAZIM®, STRATAGRAFT®, TICOVAC®, and ZEGALOGUE®. COMIRNATY®** was also omitted from the analysis due to skews in its commercial sales driven by the COVID-19 pandemic.

Brand Name (Company)	Therapeutic Area Approval	2021 Indication Approval[4]	FDA Approval Date	Reported Revenue in 2021 ($M)	Reported Revenue in 2022 ($M)	Component Scores			Overall Score
						Therapeutic Score	Commercial Score	R&D Score	
LIVTENCITY® (Takeda)	Infectious Disease	CMV infections	11/23/2021	$17	$75	4.6	1.6	1.5	2.8
VAXNEUVANCE® (Merck & Co)	Infectious Disease	Pneumococcal infection prophylaxis	07/16/2021	$2	$23	3.2	2.4	2.5	2.7
FOTIVDA® (AVEO Oncology)	Oncology	Renal cell carcinoma (RCC)	03/10/2021	$39	$107	4.0	2.2	1.0	2.7
ZYNLONTA® (ADC Therapeutics)	Oncology	Non-Hodgkin lymphoma (NHL)	04/23/2021	$40	$80	3.2	1.6	3.5	2.6
KERENDIA® (Bayer)	Nephrology	Diabetic nephropathy	07/09/2021	$23	$104	3.6	2.2	1.0	2.5
EMPAVELI® (Apellis Pharmaceuticals)	Hematology	Paroxysmal nocturnal haemoglobinuria (PNH)	5/14/2021	$15	$65	3.6	1.4	2.5	2.5
TEPMETKO® (Merck KGaA)	Oncology	Non-small cell lung cancer (NSCLC)	02/03/2021	$22	$32	4.2	1.0	2.0	2.5
ADBRY® (LEO Pharma)	Dermatology	Eczema/Dermatitis	12/27/2021	$0	$0	3.2	2.2	1.5	2.5
RYBREVANT® (Johnson & Johnson)	Oncology	Non-small cell lung cancer (NSCLC)	05/21/2021	$0	$41	4.0	1.4	1.5	2.5
TIVDAK® (Seagen)	Oncology	Cervical cancer	09/20/2021	$6	$63	4.0	1.4	1.5	2.5
VERQUVO® (Merck & Co)	Cardiology	Chronic heart failure (CHF)	01/19/2021	$9	$30	4.0	1.0	2.0	2.4
LEQVIO® (Novartis)	Cardiology	Familial hypercholesterolaemia	12/22/2021	$0	$59	3.0	2.4	1.0	2.4
SAPHNELO® (AstraZeneca)	Rheumatology	Systemic lupus erythematosus (SLE)	07/30/2021	$8	$111	3.2	2.2	1.0	2.4
EVKEEZA® (Regeneron Pharmaceuticals)	Cardiology	Familial hypercholesterolaemia	02/11/2021	$18	$49	3.0	1.6	2.5	2.3
EXKIVITY® (Takeda)	Oncology	Non-small cell lung cancer (NSCLC)	09/15/2021	$25	$24	4.0	1.0	1.5	2.3
SCEMBLIX® (Novartis)	Oncology	Leukaemia, chronic myeloid (CML)	10/29/2021	$0	$141	3.2	2.0	1.0	2.3
RETHYMIC® (Sumitomo Pharma)	Endocrine	DiGeorge syndrome	10/08/2021	$3	$33	4.4	1.0	0.0	2.2
PONVORY® (Johnson & Johnson)	Neurology	Relapsing-Remitting MS (RRMS)	03/18/2021	$21	$79	2.6	1.6	2.0	2.1
QELBREE® (Supernus Pharmaceuticals)	Psychiatry	Attention deficit disorder/hyperactivity (ADD/ADHD)	04/02/2021	$10	$61	2.8	1.4	2.0	2.1
JEMPERLI® (GSK)	Oncology	Uterine cancer	04/22/2021	$3	$16	3.2	1.2	1.0	2.0
LYBALVI® (Alkermes)	Psychiatry	Schizophrenia	05/28/2021	$4	$48	2.8	1.4	1.0	1.9
KORSUVA® (CSL)	Dermatology	Pruritus	08/23/2021	$0	$34	2.0	1.2	1.5	1.6

[4] Certain products in multi-year analysis have been approved for multiple indications since initial approval in 2021. 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 2021 products: **BESREMI®, FEXINIDAZOLE®, NULIBRY®, PREHEVBRIO®, PREVNAR 20®, RYPLAZIM®, STRATAGRAFT®, TICOVAC®, and ZEGALOGUE®. COMIRNATY®** was also omitted from the analysis due to skews in its commercial sales driven by the COVID-19 pandemic.

Figure 1: Comparison of Therapeutic and Commercial Scores for Drugs Approved by the FDA, 2021

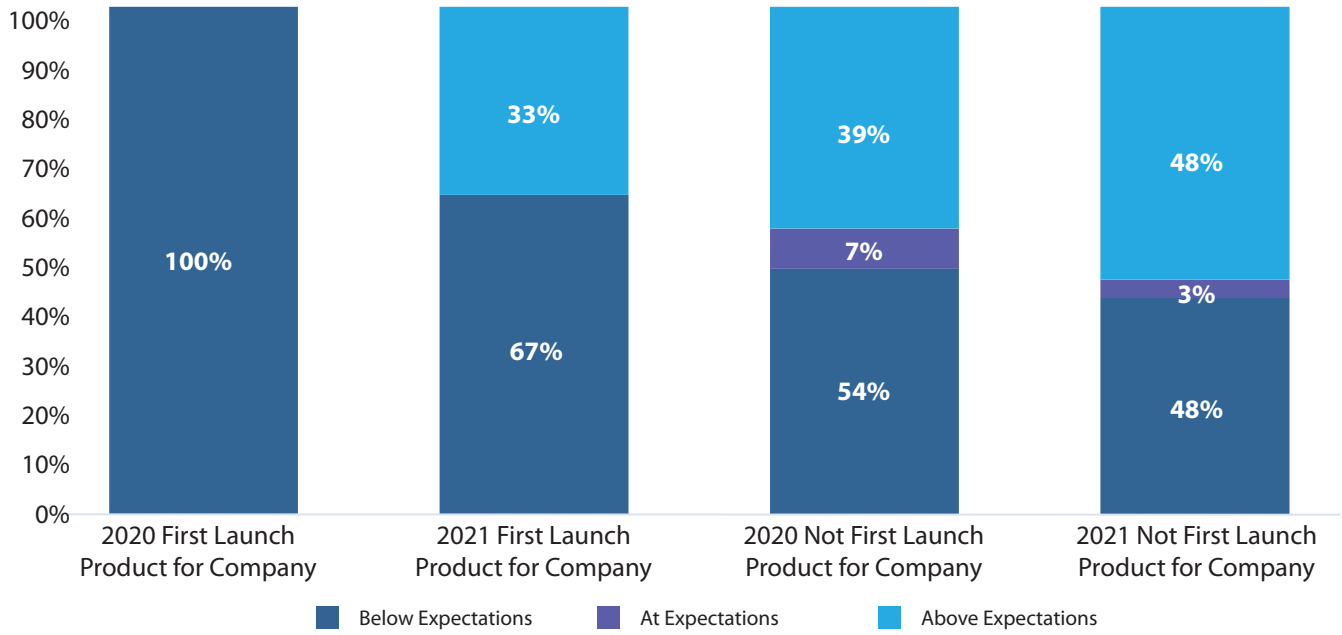
The line below is the linear regression of commercial score on therapeutics score for drugs approved by the FDA and included across all drugs approved in 2021, relative to the rest of the Drug Indices from 2016-2020.



*Includes products reviewed in previous Trinity Drug Indices from 2016-2021

Figure 2: Comparison of Commercial Performance by Product Type in 2019 vs 2020 vs 2021: "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?



Case Studies

The Trinity team performed two sets of case studies to elucidate perspectives for driving commercial success. In the first set, we analyzed the performance of the latest oncology CAR-T approvals, BREYANZI® and ABECMA®, to see if manufacturers took away lessons from the launches of YESCARTA® and KYMRIAH® to improve launch outcomes. In the second set of case studies, the top three 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.

CAR-T Case Study: ABECMA® and BREYANZI®

An uptick in CAR-T investment allowed ABECMA to pave the way in multiple myeloma and BREYANZI to shine through in a crowded diffuse large B-cell lymphoma (DLBCL) marketplace, but manufacturing hurdles slowed initial uptake for both products.

ABECMA was the first CAR-T therapy to be launched for multiple myeloma, initially approved for 5L+ R/R and later expanded to 3L+ R/R in 2024. Like other CAR-Ts, ABECMA carried risks of neurotoxicity and cytokine release syndrome (CRS), a potentially life-threatening acute systemic inflammatory syndrome. Due to these safety concerns, the product had a boxed warning and stringent monitoring requirements for seven days post-infusion. Despite these requirements, ABECMA saw high demand upon launch, but supply and manufacturing bottlenecks initially hindered its uptake. The initial excitement around ABECMA was driven by its robust and differentiated efficacy profile of >2x ORR benefits and prolonged OS compared to standard of care. Academic centers were particularly ready for patient monitoring and CRS management, and academic hematologist oncologists were already familiar with CAR-T therapies like YESCARTA and KYMRIAH in DLBCL.

However, BMS faced major challenges when CARVYKTI® launched one year later with superior clinical efficacy benefits (CARVYKTI launch price: ~$465K, ABECMA ~$419K at launch). In addition to superior clinical data, CARVYKTI received label expansion into 2L+ soon after ABECMA expanded its label to 3L+, further contributing to CARVYKTI's uptake ahead of ABECMA. By 2023, CARVYKTI's U.S. sales were already $469M compared to ABECMA's $358M, making CARVYKTI the projected market leader in the multiple myeloma CAR-T space in the coming years. The subsequent launch of several T-cell engagers (TCEs) from 2022 onwards, such as TECVAYLI®, TALVEY®, and ELREXFIO®, has continued to limit ABECMA's uptake, particularly in the community setting. These TCEs have shown favorable efficacy with superior safety (lower/less severe CRS risk) and less burdensome monitoring requirements, leading to greater uptake in the community, where a majority of patients are treated. Overall, the CAR-T class share in multiple myeloma will likely continue growing in future due to its longer market presence and proven efficacy, with CARVYKTI at the forefront of this growth.

Where ABECMA struggled in multiple myeloma, BMS has made inroads in the DLBCL market with BREYANZI despite being third to market after YESCARTA and KYMRIAH, which have a years-long head start (launched in 2017 and 2018, respectively). BREYANZI's best-in-class profile, notably driven by superior safety (lower/milder CRS risk), has been a key factor in its market penetration. YESCARTA's role in setting up the CAR-T infrastructure benefited both KYMRIAH and BREYANZI. However, BMS's capacity issues for ABECMA persisted when rolling out BREYANZI as demand outpaced supply slowing initial uptake. While BREYANZI's share of CAR-Ts in DLBCL is expected to increase, it still has a long way to go to catch up to YESCARTA's sales. YESCARTA's longer presence in the market, availability of long-term data with proven efficacy, and the familiarity and comfort it has established with healthcare professionals will continue to drive sales.

Case Studies

VYVGART® (Drug of the Year)

Background: Generalized myasthenia gravis (gMG) is a chronic autoimmune neuromuscular condition that had few targeted treatment options prior to VYVGART's launch in late 2021. Though mortality rate from gMG is extremely low, worsening of symptoms and/or comorbidity development can lead to significant deterioration in quality of life and need for urgent care (i.e., myasthenic crises requiring hospitalization, intubation and possibly death). VYVGART offered a safer, more efficacious and more convenient advanced therapy option given its novel neonatal fragment crystallizable receptor for IgG (FcRN) mechanism of action, compared to the C5 inhibitor SOLIRIS®. Since the launch of VYVGART, numerous products have entered the advanced market including ULTOMIRIS® (Alexion/AstraZeneca) and RYSTIGGO® and ZILBRYSQ® (UCB). Furthermore, gMG has become a hot area for the initial focus of cell therapy companies to bring CAR-T technology into autoimmune conditions.

Results: Despite being argenx's first launch, the company successfully navigated VYVGART's launch against competition from big pharma in the form of SOLIRIS, exceeding analyst expectations and quickly overtaking other later lines of treatment (i.e., rituximab, IVIg). VYVGART eclipsed blockbuster status in its second year and remains the market leader despite ongoing competition (with upcoming competition from Johnson & Johnson's nipocalimab). While the company faced some headwinds from the COVID pandemic, argenx invested heavily in the launch including HCP targeting and DTC to drive disease awareness and use of advanced therapies (i.e., increasing number of patients that enter the funnel). Argenx invested significantly higher amounts in SG&A for the launch of VYVGART compared to other first-launch companies due to the competitive nature of the gMG market and goal for establishing a robust foundation for future label expansions, including follow-on indications and formulations. VYVGART is anticipated to surpass $2B+ in U.S. sales by 2028 and has received approvals in other conditions including ITP in March 2024 (Japan only) and CIDP June 2024. Additionally, it is being studied in other autoimmune conditions like myositis and thyroid eye disease (TED), bolstering the opportunity for the company to strengthen its leadership in the autoimmune space with this pipeline in an asset.

Commercial Learnings: Argenx's stance for their first launch centered on an "all-in" mentality, investing heavily throughout the pre-launch and launch year to ensure they could achieve physician engagement of the ~7,700 addressable U.S. neurologists. Given the use of common products across autoimmune conditions (such as steroids, IVIg, rituximab and SOLIRIS®), it was important for argenx to focus on in-person physician education to grow prescriber awareness. Furthermore, they prioritized recruiting high-volume prescribers to establish a strong foundation that would help fend off competition backed by big pharmaceutical competitors. Finally, argenx focused on patient identification and engagement, and amplifying patient voices given the lack of advanced treatments. Consequently, argenx has significantly grown the advanced treatment penetration into the gMG market.

Case Studies

CABENUVA® (Runner-Up Drug of the Year)

Background: HIV is a lifelong viral illness that is immunocompromising, can easily spread and if left untreated can be life threatening. By 2020, with a prevalence of nearly 1.2 million in the U.S. and nearly 40 million worldwide, the HIV therapy market was saturated with both generic and branded therapies in the form of oral therapies that are administered daily. CABENUVA was initially approved in January 2021 as a once-monthly treatment for HIV-1 in virologically suppressed adults becoming the first and only complete long-acting HIV treatment regimen.

Results: CABENUVA had relatively slower uptake due to the impact of the COVID-19 pandemic, but with the pandemic receding and a less frequent dose of CABENUVA being approved in February of 2022, ViiV has been hopeful that CABENUVA can gain additional market traction. Despite facing these early headwinds along with the logistical issues of injections and high satisfaction with HIV orals, CABENUVA has steadily grown, slowly eating into the share of daily oral therapies. In 2023, CABENUVA achieved $730M in U.S. sales, with 2030 forecasted sales projected to be greater than $1.86B annually. Despite Gilead's BIKTARVY® continuing to lead the HIV market with nearly 45% market share, ViiV recently ran their SOLAR trial showing CABENUVA's noninferiority to daily BIKTARVY in parallel with studies showing that patient who switch to CABENUVA are happier than those who remain on oral BIKTARVY. By continuing to challenge Gilead head on and show the promise of a non-daily therapy, CABENUVA has been able to plant its foot in the HIV market.

Commercial Learnings: With the development of CABENUVA, ViiV provided patients with an alternative therapy that eliminates the need for daily medication. With extremely high rates of patient treatment fatigue, ViiV was able to alleviate a significant patient burden and give them the promise at a better future. Initially, ViiV designed CABENUVA to target non-compliant patients, however they soon came to understand that pill fatigue in the HIV community was extremely high. By combining a face-to-face approach from sales reps targeting HIV advocacy activities with a digital DTC marketing campaign showing patient experiences switching to CABENUVA, ViiV was able to achieve a successful launch of the product. After launch, sales teams continued to raise awareness, provide educational tools and offer one-month oral lead-in therapies to ease the transition and logistical burden of an injectable therapy. Ultimately, by focusing on a new route of administration for a disease that has a significant psychological burden, ViiV was able to successfully break through a crowded HIV market and continues to see growth year-over-year.

Case Studies

LUMAKRAS® (#3 Drug of the Year)

Background: Prior to the launch of LUMAKRAS in May 2021, there were no targeted therapies available for non-small cell lung cancer (NSCLC) patients harboring a $KRAS^{G12C}$ mutation. NSCLC is the most common form of lung cancer (~85%) and represents one of the largest markets in oncology, accounting for ~200-250K annual incident patients and ~$15B+ in net sales in the U.S. in 2023. In the last 5-10 years, the NSCLC market has become increasingly segmented, following myriad targeted therapy approvals for subgroups of patients with specific driver mutations[5]: EGFR mutation/insertion, ALK rearrangement, ROS-1 rearrangement, RET fusion, BRAF mutation, MET mutation, $KRAS^{G12C}$ mutation and more recently HER2 mutation. The success of these targeted therapies is predicated on delivering a survival benefit to a subset of biomarker-selected patients over the options offered to the "non-driver mutation" population, which in NSCLC most commonly features PD-(L)1 +/- Chemo followed by VEGF +/- Chemo. As the first approved KRAS inhibitor, LUMAKRAS created a market for the ~10-15% of NSCLC patients with a $KRAS^{G12C}$ mutation who would have otherwise been treated according to the "non-driver mutation" catchall paradigm, demonstrating a breakthrough success against what had long been considered an undruggable target.[6]

Results: Despite widespread enthusiasm for LUMAKRAS availability at the time of U.S. launch, commercial performance did not meet expectations in the product's first two calendar years as the first and only approved therapy for $KRAS^{G12C}$ patients, cumulatively totaling <$350M in the U.S. The annualized revenue trend was even more troubling, with total U.S. sales in 2023 nominally decreasing relative to the prior year ($222M vs $197M in 2022). While LUMAKRAS clinical profile includes some drawbacks (e.g., tolerability) that could have contributed to mismatched demand relative to original expectations, the culprit is more likely nuances in patient identification. Many market creators face headwinds in identifying eligible patients, but non-rare oncology may not immediately jump to mind as a space where this hurdle would play an outsized role, given how standard and widespread biomarker testing is today. Within LUMAKRAS's first year and a half on the market, Amgen reported the product was being used to treat the vast majority (~85%) of $KRAS^{G12C}$ mutated patients whose oncologists had their KRAS test results available; however, they learned that oncologists only had these results when a patient failed their initial treatment around half of the time.[6] While biomarker testing is largely reflexive at time of metastatic NSCLC diagnosis, LUMAKRAS is only available for patients in the 2L+ setting. These challenges have also been compounded by recent clinical/regulatory failures, including Amgen scrapping plans for a 1L PD-(L)1 combo due to safety/tolerability data in late 2022 and FDA rejection of full approval in the original go-to-market indication in late 2023. However, Amgen is hopeful that expansion to new markets will drive additional growth, and the FDA's decision to green-light LUMAKRAS in combination with VECTIBIX® for the treatment of colorectal cancer as of Jan 16, 2025 is an auspicious start to the new year.

Commercial Learnings: NSCLC is a common target for pharma and biotech developers alike given the sheer size of the eligible population, with the thesis that even capturing a right-to-win within a small subset of the overall market is commercially attractive. For Amgen, this seems likely to have held true, even in spite of the challenges noted above, with LUMAKRAS having now generated over $900M in total U.S. revenue to date and projected to eventually achieve that mark annually by the end of the decade driven by growth of the $KRAS^{G12C}$ class. Despite subsequent expansion failures in NSCLC and being beaten to other tumors by BMS's KRAZATI®, LUMAKRAS has laid the foundation for a now established and expanding KRAS class, once considered potentially unattainable. The case of LUMAKRAS represents an inflection point in therapeutic advancement against a key oncogenic target and indicates the importance of considering nuances in the patient journey that may impact identification when building a new biomarker-directed niche in oncology. Subsequent indication expansions planned for LUMAKRAS will help tell the full picture of the product's commercial value, but the first 2-3 year rollercoaster still provide some useful lessons in the meantime.

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[5] Later-line/salvage NSCLC patients may benefit from other pan-tumor-indicated biomarker-directed approaches, such as NTRK gene fusions (ROZLYTREK®, VITRAKVI®) and high tumor mutational burden (KEYTRUDA®)

[6] For decades, KRAS was broadly considered undruggable given the lack of classic drug binding sites

[7] https://www.fiercepharma.com/marketing/amgen-outlines-lumakras-newly-diagnosed-lung-cancer-plan-kras-launch-hits-snag

LOOKING AHEAD TO 2022 APPROVALS

In 2022, there were a combined **44 novel drug and biological license application approvals,** an ongoing upward trend over the past 6 years. Noteworthy approvals included the first targeted radioligand therapy (PLUVICTO®), the first-in-class allosteric tyrosine kinase 2 (TYK2) inhibitor (SOTYKTU®) and a host of episomal transfer gene therapies like HEMGENIX®, SKYSONA® and ZYNTEGLO®. New approvals span a wide array of therapeutics areas including oncology (~30%) and neurology (~9%). Additionally, ~70% of approvals received orphan drug designation. We look forward to profiling the innovations of 2022.

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

40%

Commercial consists of

- How well the product has performed first three years following launch (40%)
- The latest sales expectations over the next four years (40%)
- How well the product is doing compared to its original sales expectations over the first two years post-launch (20%)

40%

Therapeutic consists of an internal Trinity survey sent to managers and leadership team in order to understand

- How well each drug compares to prior SOC (60%)
- Level of unmet need in indication (20%)
- The novelty of the drug based on its modality, technology, and overall clinical profile (20%)

20%

R&D consists of

- Total number of patients enrolled across all trials supporting regulatory approval, adjusted for relative trial cost by therapeutic area (50%)
- Total duration of clinical development from phase I to approval (50%)

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About Trinity

With almost 30 years of expertise, a best-in-the-business team and unrivaled access to data and analytics, Trinity Life Sciences is a modern partner to companies in the life sciences industry. Trinity combines strategy, insights and analytics to help life science executives with clinical and commercial decision-making. We serve over 300 pharmaceutical, biotech and medical device clients, helping them develop the right drugs and devices for today's market and optimize them once in market. We have a diverse staff of over 1200 people and 11 global offices across the U.S., Europe and Asia. Ultimately, we know that every decision our clients make impacts a life, and when we help our clients achieve their goals, the world benefits. To learn more about how Trinity is elevating the industry and driving evidence to action, visit trinitylifesciences.com.

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