TRINITY

TRINITY Drug Index

2019 Trinity Drug Index Evaluates Actual Commercial Performance of Novel Drugs Approved in 2016

Fewer Approvals, but Neurology Rivals Oncology and Sees Major Innovations

Dave Fitzhenry, Van Sandwick, Eli Leavitt, RJ Rovner, Lisa Li,

Gavin Miyasato, Neal Dunn, Leslie Sandberg Orne

Published: January 2020

INTRODUCTION

This report, the fourth 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. It provides a comprehensive evaluation of the performance of novel drugs approved by the FDA in 2016, scoring each on its commercial performance, therapeutic value, and R&D investment (Table 1: Drug ranking – Ratings on a 1-5 scale).

Although only 26 unique therapeutic agents approved by CDER and CBER (Centers for Drug and Biologics Evaluation & Research) in 2016 were profiled in this Index, compared to the 50+ profiled in the Trinity Drug Index reports for the two previous years, the approvals signaled key trends. Of the 26, half were biologic products, including novel nucleic acid and cell-based therapies. In addition, neurology approvals represented ~20% of the total, while metabolic and oncology each accounted for 15% of total approvals. By comparison, oncology drugs represented 30% of approvals in 2015, according to the 2018 Trinity Drug Index.

Key themes and emerging trends across the industry, including the relative increase in neurology products as a percentage of total approvals, are highlighted in the 2019 Trinity Drug Index.

2016 DRUG APPROVAL HIGHLIGHTS

1 **Unlike prior years, 2016 saw neurology outpace oncology in terms of percent of total approvals, representing two of the five highest scoring products in this year's cohort. In addition to oncology and neurology, infectious disease products saw an uptick in approvals, which included the second highest scoring product on this year's Index (EPCLUSA®).**

Neurology Approvals
~20% (5/26)

Infectious Disease Approvals
~20% (5/26)

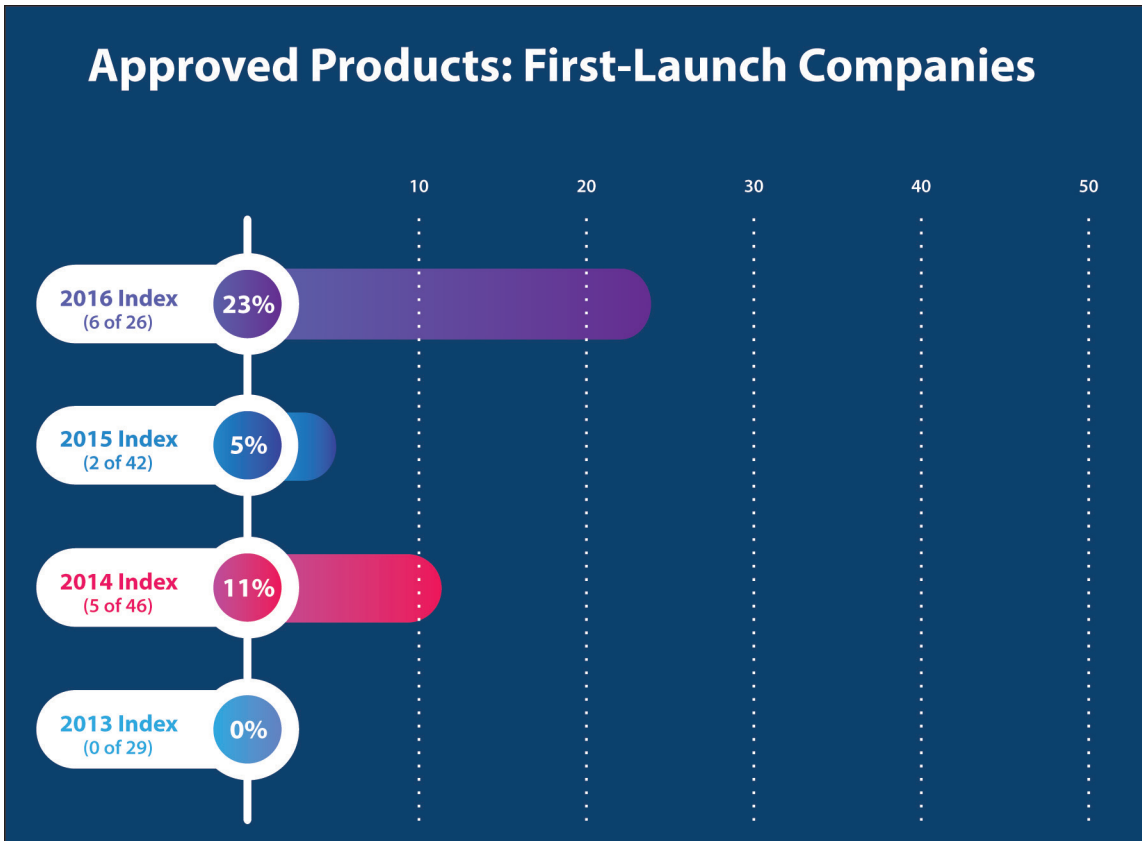
Oncology Approvals
~15% (4/26)

2 **In addition to the relative uptick in neurology approvals as a percentage of 2016 total approvals, two highly innovative anti-sense oligonucleotide products were approved for rare degenerative neurologic indications (EXONDYS 51® and SPINRAZA®). Both of these products performed well commercially compared to the other products approved in 2016.**

SPINRAZA, a novel approach to treating SMA (spinal muscular atrophy), was the highest rated product on this year's Index. We profile the key success factors and details surrounding this product in depth as a case study.

EXONDYS 51, a novel approach to treating DMD (Duchenne muscular dystrophy) based on exon-skipping, was the fifth ranked product on our Index, driven by its high therapeutic score. Additionally, EXONDYS 51 is one of the products profiled as part of our analysis of companies launching their first product.

3 **Finally, we tabulated the percentage of products that constituted a "first launch" for their respective companies in 2016, relative to products included in previous annual Indices. The results are quite interesting as the cohort of profiled products from 2016 featured significantly more first-launch companies as a percentage of total approvals compared to the prior years.**



DRUG RANKING

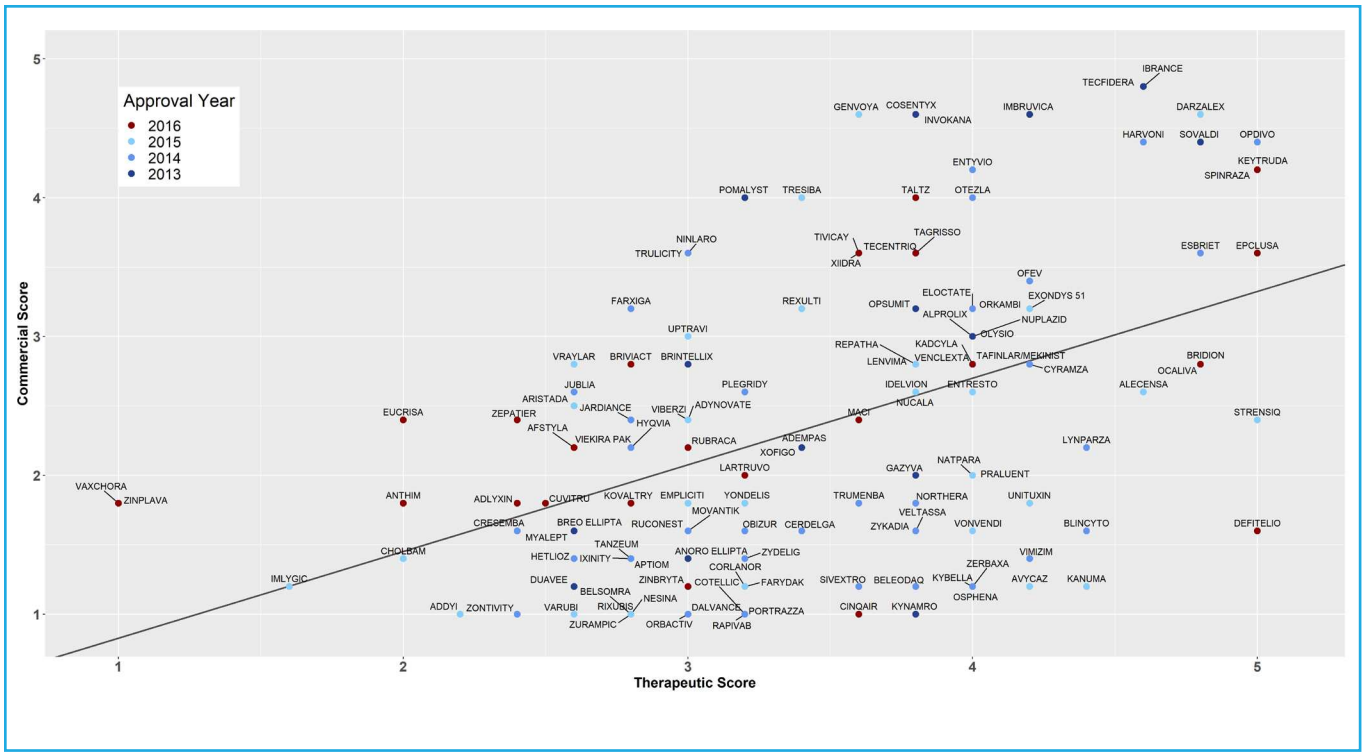
The overall and component scores for each drug are shown in Table 1 (*see page 6*). As with each of the prior Indices, the three component scores for each of the products were informed by an internal survey of Trinity leadership and managers to assess therapeutic value, an analysis of expected versus 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 2016 Approval	Component Scores			Overall Score
		Therapeutic	Commercial	R&D	
SPINRAZA® (Biogen)	Neurology	5.0	4.2	4.5	4.6
EPCLUSA® (Gilead)	Infectious Disease	5.0	3.6	4.0	4.2
TECENTRIQ® (Roche)	Oncology	3.8	3.6	5.0	4.0
OCALIVA® (Intercept)	Hepatology	4.8	2.8	4.0	3.8
EXONDYS 51® (Sarepta)	Neurology	4.2	3.2	3.5	3.7
TALTZ® (Eli Lilly)	Dermatology	3.8	4.0	2.5	3.6
VENCLEXTA® (AbbVie/Genentech)	Oncology	4.0	2.8	4.0	3.5
NUPLAZID® (Acadia)	Neurology	4.0	3.0	3.5	3.5
XIIDRA® (Shire)	Ophthalmology	3.6	3.6	3.0	3.5
IDELVION® (CSL Behring)	Hematology	3.8	2.6	4.5	3.5
MACI® (Vericel)	Orthopedics	3.6	2.4	5.0	3.4
DEFITELIO® (Jazz Pharmaceuticals)	Hepatology	5.0	1.6	3.0	3.2
RUBRACA® (Clovis Oncology)	Oncology	3.0	2.2	4.5	3.0
AFSTYLA® (CSL Behring)	Hematology	2.6	2.2	5.0	2.9
LARTRUVO® (Eli Lilly)*	Oncology	3.2	2.0	3.5	2.8
BRIVIACT® (UCB)	Neurology	2.8	2.8	2.5	2.7
KOVALTRY® (Bayer)	Hematology	2.8	1.8	4.5	2.7
ZEPATIER® (Merck)	Infectious Disease	2.4	2.4	4.0	2.7
CINQAIR® (Teva)	Pulmonology	3.6	1.0	4.0	2.6
CUVITRU (Takeda)	Immunology	2.5	1.8	4.5	2.6
EUCRISA® (Pfizer)	Dermatology	2.0	2.4	2.5	2.3
ANTHIM® (Elusys)	Infectious Disease	2.0	1.8	3.5	2.2
ZINBRYTA (Biogen/AbbVie)*	Neurology	3.0	1.2	2.5	2.2
ADLYXIN® (Sanofi)	Metabolic	2.4	1.8	1.0	1.9
VAXCHORA (Emergent Biosolutions)	Infectious Disease	1.0	1.8	3.5	1.8
ZINPLAVA® (Merck)	Infectious Disease	1.0	1.8	3.0	1.7

FIGURE 1: Comparison of therapeutic and commercial scores for drugs approved by the FDA, 2013-2016

The line below is the linear regression of commercial score on therapeutic score for drugs approved by the FDA and included across all of the Trinity Drug Indices.



See Table 1

[1] Certain products in the multi-year analysis overlap. As such, we have indicated the most recent approvals first. Please note that this applies to the following 2016 products: NUCALA®, TIVICAY®, TAGRISSO®, BRIDION®, KEYTRUDA®, TAFINLAR®/MEKINIST®, KADCYLA®, OLYSIO (product has been discontinued), ALPROLIX®.

* Product has been discontinued.

KEY THEMES

COMMERCIAL PERFORMANCE

Products approved in 2016 were closer to the annual trend-line of commercial performance as a function of therapeutic value, as well as to the historical trend of all products approved from 2013 through 2016, implying their therapeutic value translated more directly into commercial performance.

2016 showed fewer outliers than in prior years; more products achieved the commercial performance expected based on their therapeutic value. On one hand, this leaves us with fewer exciting over-performers, the commercial breakthroughs that outperformed based on their therapeutic story at launch. On the other hand, we see fewer under-performers, begging the question: is tighter correlation to the Index trend-line indicative of more efficient drug development thinking, and if so, is this a trend we may continue to see?

For example, in prior years, we have reported on orphan products and expensive antibiotics that had high therapeutic value but did not perform well commercially due to numerous market pressures; in 2016, we see fewer products with a strong therapeutic value but no commercial home.

HIGH PERFORMERS

SPINRAZA was the highest performing product in the 2016 Index, followed by EPCLUSA.

SPINRAZA was the best performer in the therapeutic and commercial assessment, driven by its high therapeutic value for previously untreatable SMA patients and successful

commercial launch. As we detail in the case study, Biogen paired a product addressing a true unmet medical need with proactive commercial planning and thoughtful execution.

EPCLUSA was a top performer, despite slightly missing analyst projections, based on the billions of dollars in revenue it was able to capture in the crowded HCV (Hepatitis C virus) market as the first product with label claims for all six HCV genotypes. More specifically, revenue erosion in 2018 due to newly launched pan-genotype HCV products (e.g., MAVYRET™) was counterbalanced by strong commercial performance from launch. EPCLUSA's strong therapeutic score as the first pan-genotype approach, paired with a successful launch, elevated it to the top of our list.

NEUROLOGY INNOVATIONS

Neurology products approved in 2016 spanned the gamut of commercial and clinical performance, with some highly innovative products for untapped indications and some more traditional approaches for established markets.

Innovative approaches including SPINRAZA, EXONDYS 51, and NUPLAZID® (a novel approach to treating hallucinations and delusions associated with Parkinson's disease psychosis) were near the top of our Drug Index, mainly powered by their high therapeutic scores. Aside from SPINRAZA, commercial performance for these novel neurology products did not significantly exceed expectations based on our Index of products approved from 2013 to 2016. We'll touch on all three of these products in more depth in our case studies on SPINRAZA and selected "first launch" products (including EXONDYS 51 and NUPLAZID).

Additional approaches for established markets had more mixed results. BRIVIACT® (a moderately differentiated product in the same class as the leading anti-psychotic medication KEPPRA®) outperformed commercially compared to its middling therapeutic score, while ZINBRYTA® (a repurposed oncology product for later line multiple sclerosis with a higher therapeutic score than BRIVIACT) was a commercial failure and was eventually pulled from the market in March 2018 due to safety issues.

CASE STUDIES

SPINRAZA

Biogen's disease-modifying antisense oglionucleotide therapy, SPINRAZA, revolutionized the treatment of SMA, a leading genetic cause of death in infants and toddlers. Strong positioning as the first and only therapy for SMA with clinical data demonstrating significant disease benefit, along with a considerable push for market access, helped SPINRAZA generate sales, outpacing early expectations. SPINRAZA demonstrates a case for thoughtful strategy driving commercial success for a high-cost innovative therapy.

Background

The launch of SPINRAZA brought considerable hope for the SMA community. The therapy fell under the spotlight of payer criticism, however, given its high US sticker price of $750,000 for the first year of treatment and $375,000 for each year thereafter. Despite this, SPINRAZA demonstrated clinical benefit and first-to-market positioning in a life-threatening disease affecting children, thereby garnering coverage for patients with SMA types 1 through 3 among most of the major US payers. In ex-US markets, Biogen drove access through one of the largest global pre-approval Expanded Access Programs in any rare disease, providing access to therapy free of charge. As novel therapies, such as gene therapy, launch for SMA, Biogen has continued to think ahead of the SMA market and proactively seek solutions to overcome competitive hurdles.

Results

SPINRAZA's early action in identifying and mitigating potential headwinds helped alleviate significant barriers for commercial uptake. To date, Biogen has successfully negotiated approval and access for SPINRAZA in over 40 countries, and the therapy has been used to treat more than 6,600 SMA patients. Biogen expects these numbers to keep growing as they continue to push for incremental access in clearly targeted SMA patients.

Commercial Learnings

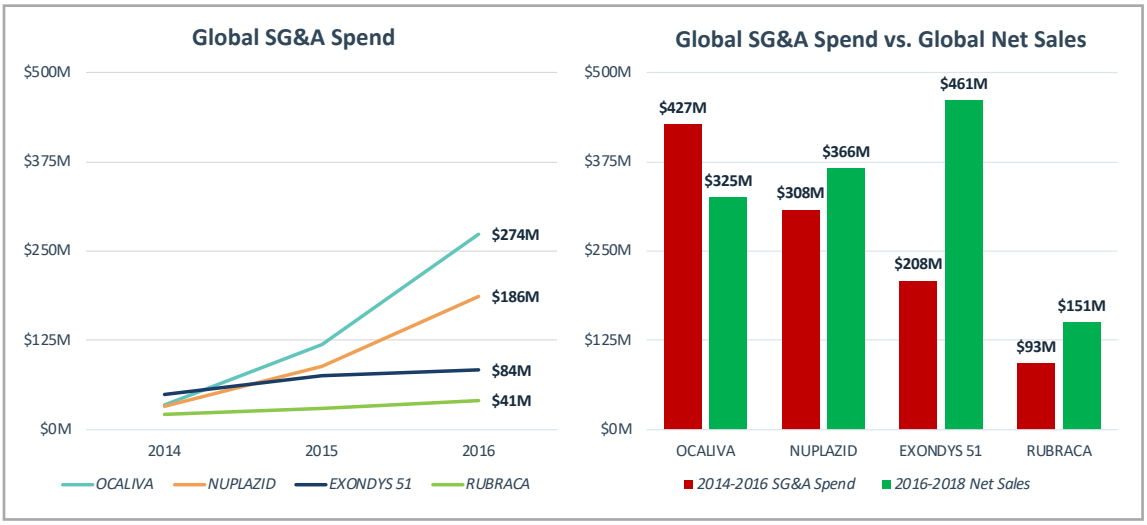
Innovative therapies, particularly those at the top of the price spectrum, can face significant commercial challenges. Strategic planning through thoughtful market research and shaping ahead of launch, however, can help products better realize their commercial value. Continued understanding of changing disease landscapes is also vital for maintaining commercial success of a product as additional therapies are approved over time and market competition continues to grow.

PROFILES OF FOUR FIRST-LAUNCH COMPANIES

Different approaches among four first-launch companies showed varying results.

Intercept (OCALIVA®), Sarepta (EXONDYS 51), Acadia (NUPLAZID), and Clovis (RUBRACA®) were all tasked with launching their first commercial product in 2016 – an exciting, high-stakes, process that brings the culmination of years of hard work and the beginning of a new chapter in the life of each company. Deciding how to utilize resources pre-launch is a complex problem with no one-size-fits-all solution. We investigated different spending approaches employed by these companies, as viewed through SG&A (Selling, General & Administrative Expenses), and results seen so far. These case studies illustrate the importance of understanding your market and brand goals, and executing a thoughtful investment strategy.

FIGURE 2: Global pre-launch SG&A spend (2014-2016) and initial global product sales (2016-2018) for 2016's four first-launch companies



Steep spending for larger markets

OCALIVA

Intercept spent aggressively pre-launch, totaling ~$430M in 2014-2016 SG&A spend, ramping up sharply year-over-year. OCALIVA, indicated for PBC (primary biliary cholangitis), was valued highly given its potential in NASH (non-alcoholic steatohepatitis), a much more prevalent indication with no treatment options. Pre-launch spending likely reflects efforts to position OCALIVA as a lead asset in development for a broader NASH opportunity. However, without successive NASH indications and follow-through on initial hopes as of yet, spending seems mismatched with commercial results, totaling ~$325M in net sales for 2016-2018 (~75% of pre-launch spend).

NUPLAZID

Acadia similarly ramped up SG&A spending pre-launch, putting a combined ~$310M into their efforts from 2014-2016. NUPLAZID targeted and gained an indication within a niche of the Parkinson's disease population, while also hoping for a substantial label expansion into the broader dementia patient pool, similar to the expansion plans for OCALIVA. In contrast to Intercept, Acadia was able to match their marketing spend to their initial indication rather than wait for a label expansion. They have seen a commensurate return, bringing in ~$365M in net sales for 2016-2018 (~120% of pre-launch spend).

Slower, steadier spending for narrower indications

EXONDYS 51

Sarepta was entering an ultra-orphan disease space in DMD after a long and uncertain regulatory road. From 2014-2016, Sarepta spent ~$210M in SG&A with a rather flat progression in annual spend. They were able to focus on and target the close-knit and engaged DMD community quickly, building narrower but deeper relationships over time, resulting in a more efficient overall launch. And Sarepta's approach has paid off to the tune of ~$460M in net sales for 2016-2018 (~220% of pre-launch spend).

RUBRACA

Clovis was not targeting a population nearly as small as Sarepta, but they also did not need to create a market or educate the stakeholders for the first time, resulting in a streamlined, steady SG&A spend totaling ~$95M from 2014-2016. RUBRACA entered the BRCA-mutant ovarian cancer market as the second PARP (poly ADP-ribose polymerase) inhibitor, 2 years after LYNPARZA® was granted approval. Clovis was able to benefit from market-shaping and education that had already taken place, being second to market. Given the fierce competition, messaging efficiency and impact would have been a key priority for the commercial team at launch, given the fight for market share and revenues to come. From 2016-2018, RUBRACA brought in ~$150M in net sales (163% of pre-launch spend), but nonetheless has been criticized for not living up to its potential.

LOOKING AHEAD TO 2017 APPROVALS

In 2017, approvals were back up, with 46 new approvals from CDER. These include products covering a wide array of disease areas.

We look forward to profiling the exciting innovations of 2017; 18 of the novel products were approved to treat orphan diseases, and 15 of the new drugs were first-in-class therapeutics.

It will be interesting to see how products aggregate around the therapeutic-commercial trendline and whether we continue to see tight correlation or have a wider spread with the increase in product volume.

Previous Trinity Drug Index Reports

2018
https://trinitylifesciences.com/wp-content/uploads/2019/05/2018_Trinity_Drug_Index_web.pdf

2017
https://trinitylifesciences.com/wp-content/uploads/2019/05/Trinity_Index_2.0.pdf

2016
https://trinitylifesciences.com/wp-content/uploads/2019/05/TRY30037Fpress.pdf

AUTHORS

Dave Fitzhenry
Chief Executive Officer | Waltham

Dave has been helping life sciences companies bring cutting edge medicines and medical devices to the market for more than two decades. Joining Trinity as Employee #3 as an Associate after college, Dave has led Trinity's growth of 20% year over year, developing and implementing best practices for new product and launch planning, due diligence for licensing and acquisitions, as well as industry-leading forecasting methods — experience that led Consulting Magazine to name him a 2017 Global Leader in Consulting.

Dave earned an AB from Harvard University.

Van Sandwick
Engagement Manager | San Francisco

Van is an Engagement Manager within the Strategic Advisory group of Trinity, with ~8 years of life science consulting and operations experience. He has been involved in numerous engagements across the strategic advisory and insights & analytics groups' core offerings, with a particular focus on corporate strategy & business development and strategic product planning.

Van holds a BS in Biological Chemistry from Bates College.

Eli Leavitt
Engagement Manager | San Francisco

Eli is an Engagement Manager within the Strategic Advisory group of Trinity, with ~5 years of experience in life science consulting. Eli has worked on a diverse set of strategic and analytic engagements across the product development timeline and spanning various therapeutic areas, with a particular focus on rare diseases and oncology.

Eli graduated cum laude from Harvard University with an AB in applied mathematics with a focus in biology.

RJ Rovner
Engagement Manager | San Francisco

RJ is an Engagement Manager within the Strategic Advisory group of Trinity. Over the last 6 years, RJ has focused predominantly in leading engagements on commercial strategy and transformation, mergers and acquisition/licensing strategy, pipeline and launch strategy, and growth marketing. RJ has a depth of experience across several therapeutic areas, but particularly hematology/oncology, immunology, neurology, and hemophilia.

RJ graduated as an Oppenheimer Scholar from the University of California, Los Angeles with a BS in Molecular, Cellular and Developmental Biology.

Lisa Li
Senior Consultant | Waltham

Lisa is a Senior Consultant within the Strategic Advisory group of Trinity. Over the course of her ~3 years of experience in life science consulting, she has supported work in a wide range of therapeutic areas and engagements. She has expertise in pricing, market access, and commercial strategy, particularly for novel therapies in hematology/oncology, immunology, neurology, and supportive care markets.

Lisa graduated from Princeton University with an AB in Biology.

Gavin Miyasato
Associate Director | Waltham

Neal Dunn
Senior Partner | Waltham

Leslie Sandberg Orne
Senior Partner & Chief Client Officer | Waltham

For more information or if you have any specific questions, please contact: Van Sandwick at vsandwick@trinitylifesciences.com

TRINITY

TRINITY Drug Index

About TRINITY

Trinity is a trusted strategic partner, providing evidence-based solutions for the life sciences. With over 20 years of experience, Trinity is committed to solving clients' most challenging problems through 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. Trinity, together with its subsidiary TGaS Advisors, has 5 offices throughout the US, including Boston, New York, Princeton, Philadelphia, and San Francisco, as well as Toronto, Canada, Gurgaon, India, and Munich, Germany. To learn more about how Trinity is elevating life sciences and driving from evidence to action, visit trinitylifesciences.com.

Contact TRINITY

CORPORATE HEADQUARTERS
230 Third Avenue
5th Floor
Waltham, MA 02451-7528

[T] +1 781-577-6300

SAN FRANCISCO
101 California Street
Suite 1550
San Francisco, CA 94111

[T] +1 781-577-6300