TRINITY

Launching During COVID-19

Assessing the Damage and Finding Success

Executive Summary

What is and isn't working for drug launches amid COVID-19? Six months after COVID-19 lockdowns began, Trinity has uncovered some surprising (and some concerning) answers to key questions everyone is asking.

Key Questions	Trinity's Answer
Is it possible to successfully launch a new product during COVID-19?	Yes, but it's not easy. Some companies in severe disease markets with limited treatment alternatives are seeing success via early market shaping to drive patient demand. Brands outside of oncology and rare disease had a more difficult first half with only one exceeding forecast and six attaining no more than 56% of forecast.
Can launches that fell short of expectations improve performance in the coming months?	Maybe. There are some early signs for companies who have effectively pivoted to novel approaches to reach stakeholders – telehealth, DTC campaigns, copay support. These strategies could allow those launches to rebound later in 2020, as we expect the typical launch success barometers at six months to get pushed out as far as 12 months in a COVID normal.
Did a requirement for HCP administration of a drug present an obstacle to new patient starts?	Surprisingly – no. But it depends on the existence of treatment alternatives.
Did anyone find success in a shift to digital and direct-to-consumer efforts?	Early signals point to yes – which raises the question: would you rather have a Kardashian or a Williams sister as your spokesperson?
What can we learn about the importance of pre-launch education and market development efforts on performance during the pandemic?	It's more vital than ever – and we haven't yet seen in full how COVID-19 impacts it. The earlier, the better!

In this paper, we examine the trajectory of new molecular entities (NMEs) approved in late 2019 and early 2020 to understand how to drive a successful launch (and avoid the pitfalls) in the age of COVID-19.

Introduction

Companies launching products right before or during the COVID-19 pandemic lockdown had to rapidly adjust their plans when field personnel could not visit HCPs in person. Major conferences shifted online, requiring changes in KOL engagement. Most critically, patients began delaying visits to HCPs or turned to (unprepared or underdeveloped) telemedicine to comply with stay-at-home orders. Every pharmaceutical company felt the impact of COVID-19 – but not every company responded with equal agility or effectiveness. Companies bringing new drugs to market in the COVID era – an era that does not yet have a clear end – will need to adjust their approaches to commercializing new drugs.

To better understand the impact of COVID-19 on recently launched drugs, we tracked the launch status of new molecular entities (NMEs) that received FDA approval between September 2019 and February 2020. A total of 28 products received approval. Of those, five delayed launch with two attributing (at least part of) their delay directly to COVID-19 (Palforzia – Aimmune; Dayvigo – Eisai).

17 products had the requisite data available to track launch performance.

NME Approvals Included in the Analysis

	Product	Company	Indication	FDA Approval date	Launch date*
Rare Disease	**Trikafta**	Vertex	CF	21-Oct-19	Oct-19
	Reblozyl	Acceleron/BMS	Beta thalassemia	8-Nov-19	Nov-19
	Adakveo	Novartis	Sickle cell disease	15-Nov-19	Dec-19
	Givlaari	Alnylam	Acute hepatic porphyria	20-Nov-19	Dec-19
	Oxbryta	GBT	Sickle cell disease	25-Nov-19	Dec-19
	Tepezza	Horizon	Thyroid Eye Disease	20-Jan-20	Feb-20
Oncology	**Padcev**	SeaGen/Astellas	Bladder cancer	18-Dec-19	Dec-19
	Enhertu	AZ / Daiichi	HER2 positive metastatic breast cancer	20-Dec-19	Jan-20
	Ayvakit	Blueprint	Gastrointestinal stromal tumor	9-Jan-20	Jan-20
	Tazverik	Epizyme	Epithelioid sarcoma and follicular lymphoma	23-Jan-20	Feb-20
Other	**Beovu**	Novartis	Wet age-related macular degeneration	8-Oct-19	Oct-19
	Caplyta	Intra-cellular	Schizophrenia	23-Dec-19	Mar-20
	Nexletol	Esperion	Hypercholesterolemia	21-Feb-20	Mar-20
	Reyvow	Lilly	Acute Migraine	11-Oct-19	Feb-20
	Ubrelvy	AbbVie/Allergan	Acute Migraine	23-Dec-19	Jan-20
	Vyepti	Lundbeck	Chronic Migraine	21-Feb-20	Apr-20
	Nurtec ODT	Biohaven	Acute Migraine	27-Feb-20	Mar-20

*Launch date is defined as the date the drug became commercially available in the US.

Sources: FDA.gov, EvaluatePharma, company websites, press releases, investor presentations, and financial disclosures

First looking at performance – there is a clear disparity. The true winner is Trikafta at nearly $2B in the first half of 2020. A few have over $100M in revenue – namely, those in severe markets with no (or very limited) treatment alternatives. Nearly half the products in our analysis haven't even reached $20M in revenue, and almost all of them are in crowded markets – migraine, gastrointestinal disorders, cardiovascular disease, psychiatry – highlighting the fact that the challenges of launching in COVID are real.

2020 YTD Performance ($MM)

We identified the following trends that shaped the trajectory of drug launches during the COVID-19 pandemic:

1. **Patients with severe diseases and/or limited alternative therapies continued to seek treatment despite COVID-19, allowing several oncology and rare disease treatments to significantly exceed consensus forecasts**
   - Brands outside of oncology and rare disease had a more difficult first half with only one exceeding forecast and six attaining approximately 50% or less of forecast

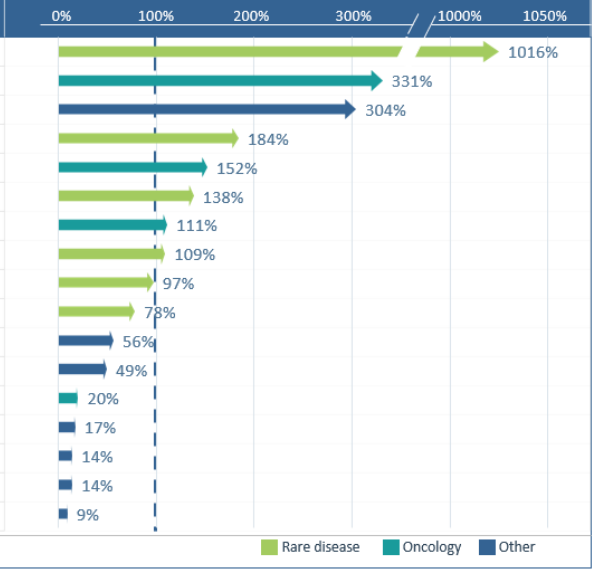
2. **HCP administration did not present an insurmountable obstacle to patient starts for newly launching agents that offered clear improvements over standard of care**

3. **Companies who were willing to make significant changes to their commercialization plans to focus on digital and direct-to-consumer efforts have shown signs of recovery and are gaining traction in crowded markets**
   - We expect elongated uptake curves for launches in more crowded and mature markets as a result of COVID-19, but whether these companies will see a full recovery by year-end is not yet clear

Performance of Drugs Approved in the Six Months Prior to COVID Against Consensus Forecast

YTD Sales Relative to Adjusted 2020 Consensus Forecast: by TA

Product	Company	Indication	Launch Date	2020 Consensus Forecast ($M)	
Tepezza	Horizon	Thyroid Eye Disease	20-Feb	$41	1016%
Padcev	SeaGen / Astellas	Bladder cancer	19-Dec	$83	331%
Ubrelvy	AbbVie / Allergan	Acute Migraine	20-Jan	$25	304%
Trikafta	Vertex	CF	19-Oct	$1955	184%
Ayvakit	Blueprint	GI stromal tumor	20-Jan	$12	152%
Reblozyl	Acceleron / BMS	Beta thalassemia	19-Nov	$91	138%
Enhertu	AZ / Daiichi	HER2+ met. breast cancer	20-Jan	$205	111%
Oxbryta	GBT	Sickle cell disease	19-Dec	$84	109%
Adakveo	Novartis	Sickle cell disease	19-Dec	$74	97%
Givlaari	Alnylam	Acute hepatic porphyria	19-Dec	$42	78%
Beovu	Novartis	Wet AMD	19-Oct	$364	56%
Nurtec ODT	Biohaven	Acute Migraine	20-Mar	$55	49%
Tazverik	Epizyme	Epithelioid sarcoma and follicular lymphoma	20-Feb	$39	20%
Vyepti	Lundbeck	Chronic Migraine	20-Apr	$38	17%
Reyvow	Lilly	Acute Migraine	20-Feb	$70	14%
Caplyta	Intra-cellular	Schizophrenia	20-Mar	$49	14%
Nexletol	Esperion	Hypercholesterolemia	20-Mar	$42	9%



Methodology: We compared company reported sales for drugs approved prior to COVID-19, including NMEs approved by the FDA between September 2019 and February 2020 that launched no later than April 2020, against February (pre-COVID) consensus forecasts for calendar year 2020. To evaluate performance at mid-year, we compared company-reported sales to consensus forecasts, adjusting for the amount of time the drug was on the market prior to June 30. Percentages in the chart show % of estimated mid-year forecast; 100% effectively means meeting forecast.

Sources: Company-reported sales, EvaluatePharma

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Motivated Patients Continued to Seek Out New Treatments

Disease severity and lack of effective alternative therapies shaped the impact of COVID-19 on drug launches, as motivated patients sought treatment for cancer and previously undertreated rare diseases. In contrast, drugs that launched in markets with an array of treatment options and/or with less clear value propositions faced more substantial barriers to success. Of the eight products included in our analysis that exceeded forecast expectations, seven target rare diseases or oncology indications.

Horizon Therapeutics' Tepezza and BMS/Acceleron's Reblozyl – two drugs that exceeded forecast expectations for the midpoint of the year – entered their respective markets as the first drugs indicated for the conditions they treat. Tepezza treats thyroid eye disease (TED), which in severe cases can result in vision loss, and Reblozyl received its initial indication for anemia associated with beta-thalassemia, providing an alternative to risky and burdensome transfusions. Vertex's Trikafta also outperformed expectations by expanding the pool of patients eligible for disease-modifying therapy for cystic fibrosis. In each of these cases, pent-up demand prior to launch and patient motivation to seek treatment contributed to the rapid adoption of new therapies. We observed cases where demand had been driven by effective market development prior to launch, discussed in more detail in a later section.

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Similarly, new oncology drugs addressing significant unmet need outperformed consensus forecast expectations. Seattle Genetics/Astellas's Padcev – used in refractory, metastatic bladder cancer – has quickly become the standard of care for this patient segment. Blueprint's Ayvakit – treating a small but underserved patient segment – received the first approval for targeted therapy in GIST and also outperformed consensus expectations.

New oncology drugs addressing significant unmet need outperformed consensus forecast expectations.

Drugs entering more mature and competitive markets faced substantial headwinds. Most of the agents launching in mature markets such as migraine, hyperlipidemia, and schizophrenia saw relatively limited uptake during the first half of the year. Of the 11 NMEs approved in this timeframe that lacked data or delayed their launch and therefore excluded from our analysis, 8 of them were in these "other" markets as well – perhaps another signal of challenges posed by COVID. In some cases, effective responses to the challenges presented by COVID may allow these products to recover in the second half of the year; we discuss some of those responses in a later section.

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Tepezza: A Case Study

Well-Planned and Executed Market Preparation is More Critical Than Ever

For drugs that launched shortly before or during the early months of the COVID-19 pandemic, well-executed market development was critical to ensuring successful launches. Manufacturers often begin patient and physician awareness campaigns and initiatives to improve diagnosis several months or more before launch; previous research from Trinity's benchmarking division, TGaS, has shown that successful launch teams send medical science liaisons (MSLs) and market access account representatives into the field 2x earlier (~15 months pre-launch) than less successful launch teams. Horizon's Tepezza provides an example of the benefits of a comprehensive market development plan.

Factors contributing to success

Among the factors Horizon credits for its expectation-beating launch of Tepezza is the work the company did beginning in 2018, when Horizon initiated its disease awareness, market development, and market access efforts. Horizon's efforts included developing a center of excellence network that included treating physicians and infusion capabilities and building out a broader infusion network to ensure patients would be able to receive the drug. That network helped ensure patients could initiate or continue treatment by helping patients locate available infusion centers during COVID lockdowns. The company also established a TED treater network that included the mix of specialists who diagnose and manage TED patients, primarily endocrinologists and ophthalmologists. Finally, the company identified and engaged patients in unbranded digital campaigns for disease awareness well in advance of launch. For example, in June 2019, the company announced its support for Eyes on Graves, a disease education initiative for patients with Graves' disease, many of whom develop TED. Horizon effectively built the funnel well in advance to identify and get patients to see TED experts, thus priming the launch.

Factors leading to concern

It's not been all success, however, as Horizon raised concerns about continuing to enroll new patients during the remainder of 2020. In its second quarter 10Q, Horizon attributed a slowing of patient enrollment forms for Tepezza to COVID-19 and anticipated an effect on new patient starts, though the company also stated that it continues to anticipate a higher number of new patients than it did in prior estimates. These challenges underscore the importance of comprehensive market development efforts that anticipate obstacles to diagnosis, reimbursement, and administration.

2 *HCP Administration Did Not Consistently Present a Barrier to Adoption of New Agents*

In the early months of the COVID-19 pandemic in the United States, patients' visits to ambulatory clinics declined substantially. According to one estimate published by The Commonwealth Fund, total visits to ambulatory practices dropped nearly 60% by the end of March and remained substantially below baseline through much of May. Despite this decline in overall patient visits, some HCP-administered products still experienced rapid adoption by motivated and supported patients.

HCP-administered products that launched successfully likely benefited from the following factors:

- Patients with severe conditions continued to seek treatment during the lockdown phases
- Infusion centers were designated as essential and remained open, which allowed patients to continue receiving IV-administered drugs
- Some patients used home administration services for IV-administered drugs or other drugs requiring the assistance of an HCP (Givlaari and Reblozyl, agents delivered by subcutaneous injection but requiring the support of an HCP)
- Companies whose pre-launch efforts included building patient support services for HCP delivery – particularly Horizon's Tepezza - benefited from those efforts

HCP administration may have presented a more significant barrier to uptake for drugs in markets where self-administered alternatives are readily available.

Lundbeck's Vyepti launched in early April as the fourth monoclonal antibody targeting CGRP approved for migraine prophylaxis – and the only anti-CGRP antibody requiring intravenous infusion. Predecessors Emgality, Ajovy, and Aimovig are administered subcutaneously. The drug has struggled to gain share to date as patients may have been reluctant to switch prophylactic treatments during lockdown – particularly if the switch was away from a self-administered treatment to one requiring a visit to an HCP. Although Vyepti is administered relatively infrequently – every three to six months – this does not appear to be a persuasive enough point of differentiation compared with the monthly or quarterly subcutaneous injection for the other anti-CGRP antibodies.

3 *Rapid, Flexible Responses to Changing Conditions is Providing Traction in Crowded Markets*

Companies promoting newly launching drugs faced a daunting challenge as COVID-19 hit: traffic to physician offices declined sharply, and practices ceased to allow in-person visits from field personnel. Nevertheless, some companies made rapid adjustments to mitigate their loss of direct access to HCPs that upended commercialization plans.

The migraine market offers an interesting case study here, as four new drugs treating migraine launched between January and April 2020. Three of the four are indicated for the acute treatment of migraine; the fourth (Vyepti) is approved for migraine prophylaxis (discussed previously).

September 2019 – February 2020 Migraine Launches

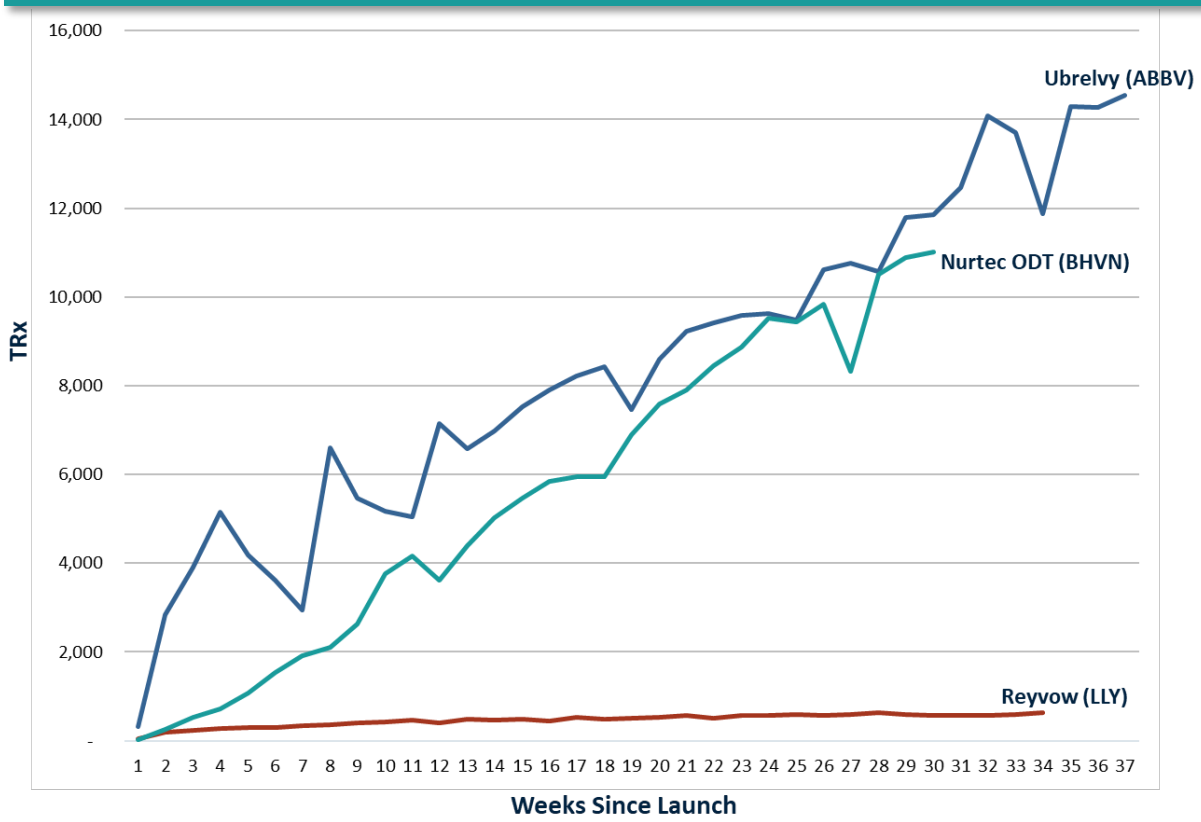
Drug	Launch Date	Indication	Mechanism of Action	Administration and Dosing
Abbvie's Ubrelvy	February 2020	Acute treatment of migraine with or without aura in adults	CGRP antagonist	Oral, as needed
Biohaven Pharmaceuticals' Nurtec ODT	March 2020	Acute treatment of migraine with or without aura in adults	CGRP antagonist	Oral, as needed
Eli Lilly's Reyvow	January 2020	Acute treatment of migraine with or without aura in adults	5HT1F receptor agonist	Oral, as needed
Lundbeck's Vyepti	April 2020	Preventive treatment of migraine in adults	CGRP antagonist	IV infusion every three months

In contrast with underserved rare diseases and oncology indications, the migraine market has more established agents entrenched in treatment, consisting of preventive, subcutaneously administered CGRP receptor antagonists indicated for migraine prevention and oral agents (primarily triptans) for acute treatment. Ubrelvy and Nurtec ODT entered the market in February and March, respectively, as the first two CGRP antagonists indicated for acute migraine and delivered orally. Eli Lilly's Reyvow, a 5-HT1F receptor agonist, offers a new mechanism of action and oral delivery.

Both Ubrelvy and Nurtec ODT entered the migraine market with the advantage of offering a mechanism already familiar to prescribing physicians from the prior launches of prophylactic CGRP antagonists and were well-positioned to become favored acute treatments for patients seeking alternatives to triptans. Ubrelvy may have also benefited from Allergan/Abbvie's prior experience marketing Botox for migraine treatment and from launching two months earlier than Nurtec ODT. The agent currently leads both Nurtec ODT and Reyvow in total prescription (TRx) volume and sales.

However, although Nurtec ODT did not meet consensus forecast at mid-year, the drug appears to be effectively gaining new patient starts and competing with Ubrelvy for share. The extent of Biohaven's effort is evidenced by over $220M in SG&A spend in the first half of 2020, further demonstrating just how competitive the migraine market is.

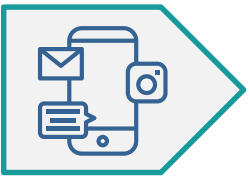
Total Prescription Volume Since Launch



Source: Symphony Health Solutions. October 2, 2020.

Nurtec ODT is Biohaven's first commercial launch, and the drug entered the market shortly before the COVID-19 pandemic reached the US. In fact, Biohaven was still building its field force for Nurtec ODT in late February when the company quickly decided to change course in response to COVID-19 by commencing its DTC campaign earlier than planned, perceiving the change as necessary to reach patients and drive new starts during lockdowns and social distancing.

Biohaven also entered into an agreement with telemedicine service Cove in April 2020 in an effort to facilitate new starts for patients who were unable to or who preferred not to visit a physician in an office setting. Cove provides specialized care and access for migraine patients through their telemedicine network, which connects patients through the Nurtec ODT website to telemedicine evaluations.



The company continued to focus resources on digital marketing and social media later in Q2, announcing social media influencer Khloe Kardashian as the spokesperson for Nurtec ODT in June. Biohaven's efforts appear to have borne fruit (albeit an expensive one); as of mid-August, Nurtec ODT continued to gain TRx share, narrowing the gap in patient share with Ubrelvy. Notably, AbbVie secured its own high-profile spokesperson in August – tennis legend Serena Williams.

Another example of how a company shifted in response to COVID

In another example of how a company shifted in response to COVID, Esperion entered the crowded and heavily genericized market for lipid-lowering agents in late March with the launch of Nexletol, as lockdown orders were initiated in much of the US. Esperion's August 2020 presentation of second-quarter results illustrated the impact of those lockdown orders, as field team contacts with HCPs remained low through much of May.

- Given the initial challenges and launch of Nexlizet in June (the follow-on combo of Nexletol and Zetia), Esperion anticipated the need to expand its use of digital outreach, and over the course of a month rolled out platforms for remote HCP interactions and digital promotional materials in an effort to replace in-person contact with HCPs as much as possible.
- The company also appears to have focused significant efforts on securing coverage with payers. As of August 2020, Esperion was reporting that both private and Medicare plans were reimbursing Nexletol, at an estimated 80% of list price for patients with private insurance and 50% for those with Medicare.
- Finally, the company mobilized its field forces quickly beginning in late May; contacts with HCPs increased substantially and prescriptions of Nexletol increased as well.

By directing the company's efforts to what was possible during Q2, Esperion may have positioned Nexletol for a much stronger Q3 (and Nexlizet for a stronger start).

For both Biohaven and Esperion, plans to rely on a traditional field force rollout and in-person contact were thwarted by COVID before they began, and neither company was able to drive sales to the extent they might have under ordinary circumstances. With an out-sized investment in marketing (approximately $90M and $220M in SG&A spend respectively for Esperion and Biohaven in the past two quarters), these companies are attempting to inject new life into their launch. In the next few months, we will see if the investment will pay off.

Early indicators in both cases suggest that their responses laid the groundwork to gain traction, elongate their uptake, and (hopefully) to see stronger performances later in the year.

Looking to the Future

The COVID-19 pandemic continues to shape companies' commercialization plans and almost certainly will through all of 2021. Companies with launches coming late in 2020 and 2021 – those whose timing place market development efforts and tactical launch preparations squarely in the COVID era – will be forced to make a significant transition from in-person activity to digital and remote activity. The COVID-19 pandemic accelerated trends already in progress such as increasing adoption of digital approaches to interacting with HCPs, KOLs, and patients. Companies with forthcoming launches need to recognize that many of the changes brought about by the COVID-19 pandemic will persist and that new modes of commercializing drugs are likely here to stay.

What is clear so far:

- The more infrastructure companies can put in place early, the more success they will have in shaping the market: developing centers of excellence, creating networks of KOLs, and facilitating access and reimbursement the foundations of this infrastructure
- Especially in non-rare, non-oncology indications where treatment alternatives exist, companies must be innovative creating in "creating space" via multiple avenues to prepare the market, find patients, and educate HCPs and payers regardless of the barriers presented by COVID-19
- Digital engagements, DTC efforts, and patient-centric activities like telehealth are showing progress
- In a recent TGaS report, 56% of companies have a dedicated group focused on how telehealth will influence their commercial organization
- Traction and ultimately success can happen regardless of your company's size, but plan for the resources (time, spend) needed to build the infrastructure and recognize the return

However, further analysis assessing the return on investment of each of these digital approaches is necessary to appropriately prioritize efforts. As this period of accelerated evolution of the drug commercialization landscape continues into 2021, Trinity will continue to provide critical insights about how to thrive in an always-shifting "normal."

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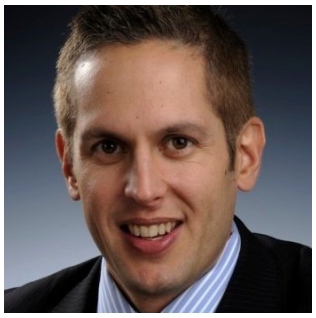

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Trinity Launch Accelerator

Trinity's Launch Accelerator platform efficiently leverages our launch activity and timing benchmarks and is customized to give you confidence in your unique launch plan build or pressure testing your plan. The platform serves as your "single source of truth" tracking tool to ensure launch success via an aligned and effective process.

Trinity EvidenceFirst

Trinity EvidenceFirst transforms the time to accessible patient level insights. Timely insights allow biopharma companies to best understand patient flow to improve patient outcomes and accelerate a potential drug's success.

Trinity CloudCast

Trinity CloudCast is the revolutionary, connected forecasting platform for life sciences companies. Forecasters can rapidly create, update, and share scenarios of their demand forecasts using the universally well-known modeling tool, Excel.

Trinity COVIDCast

For forecasters, the Trinity COVIDCast offering includes robust dynamic models of the spread and impact of COVID-19 to support decision making. It can include weekly updates to keep models informed by the latest research and data. It is Trinity CloudCast compatible.

Trinity COVIDPulse

Trinity COVIDPulse is a survey-based offering that tracks key metrics among HCPs. It produces high-level impact estimates including patient volume, treatment restrictions, and unmet needs.

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