STAT E-BOOK

Leveraging AI to automate clinical intelligence in biotech: case studies on early risk detection

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In medical parlance, "stat" means important and urgent, and that's what we're all about — quickly and smartly delivering good stories. We take you inside science labs and hospitals, biotech boardrooms, and political backrooms. We dissect crucial discoveries. We examine controversies and puncture hype. We hold individuals and institutions accountable. We introduce you to the power brokers and personalities who are driving a revolution in human health. These are the stories that matter to us all.

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Our team includes talented writers, editors, and producers capable of the kind of explanatory journalism that complicated science issues sometimes demand. And even if you don't work in science, have never stepped foot in a hospital, or hated high school biology, we've got something for you. The world of health, science, and medicine is booming and yielding fascinating stories. We explore how they affect us all. And, with our eBook series, we regularly do deep dives into timely topics to get you the inside scoop you need.

Mining the hidden signals in clinical trials.

In the last 12 months, there were over 2.5 million changes in the U.S. clinical trials registry. That equates to nearly 6,800 updates per day.

Many of these changes are expected, for instance, status or patient enrollment updates; however, deviations from the expected path make it possible to identify patterns that can anticipate trial outcomes.

Pinpointing these outliers is central to how biotech upstarts, pharmaceutical companies, and investors stay ahead of the curve of the industry's news cycles. But to do so is a time-consuming process that requires sufficient expertise in clinical development, meaning that these signals often go undetected.

STAT Trials Pulse, a new platform developed in partnership with AppliedXL, mines these hidden signals in public data to anticipate roadblocks in clinical trials. AppliedXL works with STAT journalists and other domain experts to develop specialized machine-learning algorithms that replicate the rigorous research process of biotech analysts.

The technology powering STAT Trials Pulse combines the horsepower of machine learning and the principles of investigative journalism to find signals before they become news. These early indications are a type of "pre-news" that allow professionals across the life sciences to anticipate, understand, and address potential disruptions to drug development before they become public knowledge.

This collection of articles highlights, through case stories, the impact of early detection of these red flags in drug development, and how it helps life sciences professionals to strategize and make moves ahead of the news cycle.

Anticipate risk in clinical trials months ahead of time

STAT Trials Pulse is the most advanced early warning system for clinical trial updates, trusted by the leading hedge funds, pharmaceutical companies, and biotech firms.

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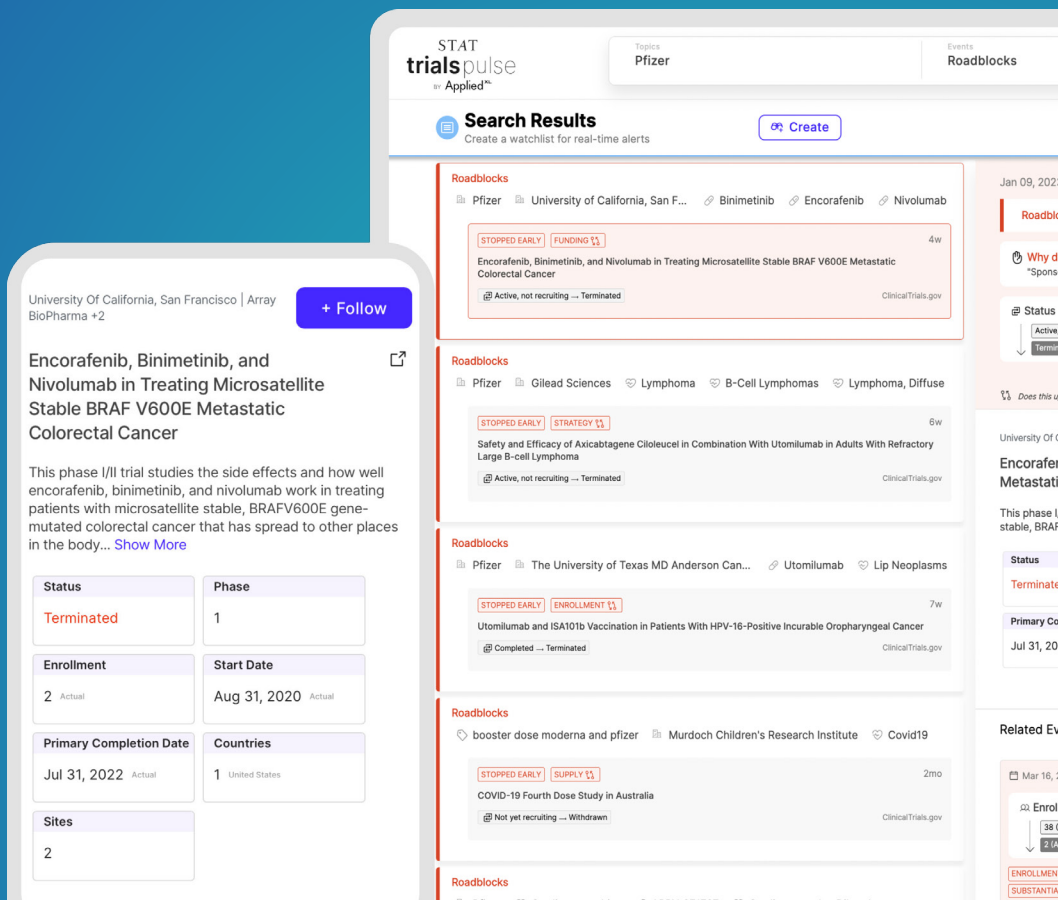

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SPONSORED INSIGHT

Early signals in Aileron Therapeutic's ALRN-6924 program hinted at a struggle for efficacy over a year before negative results

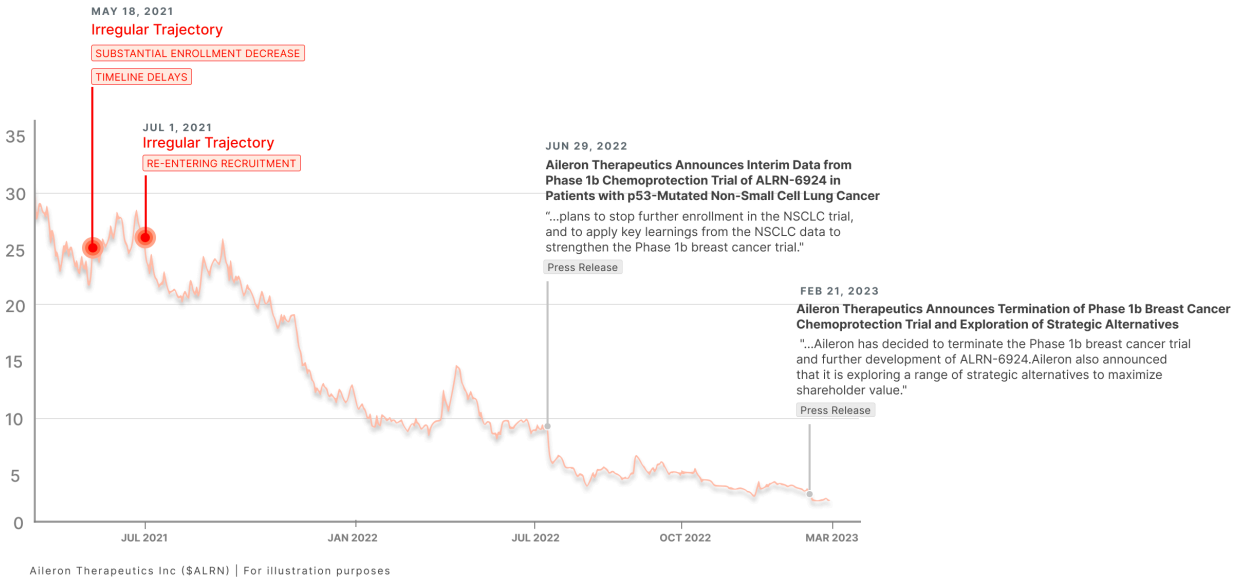
As early as May 18, 2021, STAT Trials Pulse by AppliedXL began to surface irregularities in the progression of Aileron Therapeutic's ALRN-6924 trial for chemoprotection in lung cancer, signaling a struggle for sufficient patients to determine significant efficacy. More than a year later, Aileron confirmed these red flags, terminating the trial and fueling a 41% drop in the company's stock.

Background: Aileron Therapeutics first hit the biopharma scene with a new approach to drug delivery — the potential of stapled peptides offered an enhanced ability to effectively deliver drugs to a cell, and greatly expanded the possibility of therapeutic targets that could become "druggable." With this unique first-in-class molecule came sufficient buzz – in 2017, Aileron raised $56 million in an IPO to fund the clinical development of their stapled peptide candidate, ALRN-6924.

Originally pitched as a p53-mediated tumor suppressor, ALRN-6924 began exploring both treatment of solid tumors, as well as selective chemoprotection.

In July 2019, Aileron kicked off its first trial in chemoprotection in p53-mutated lung cancer, which, when tumor suppression results flailed, became the company's sole program in development and their singular way forward.

Red flags: In mid-May 2021, a group of irregularities detected by STAT Trials Pulse surfaced red flags in the ALRN-6924 trial, serving as an early warning of potential problems within the trial.



On May 18, 2021, the trial completed enrollment with only 50% of the anticipated participants, cutting the patient count from an anticipated 120 to 60. Falling substantially below enrollment goals can change the validity of assumptions around efficacy and study design, impacting a trial's ability to achieve target power and statistically reliable results. At the same time, the primary completion date of the trial was delayed substantially, moving from the previously-anticipated March 1, 2021, to June 1, 2022.

A few months later, on July 1, 2021, the trial again varied from regular trajectory, re-entering recruitment. Often, this serves as a signal that the sponsor is looking to increase the ability to detect a signal and may be struggling for statistical significance with its current patient pool.

The impact: One year later, on June 29, 2022, Aileron announced the disappointing results of an interim analysis, highlighting that ALRN-6924 was not performing better than placebo on the exploratory composite primary endpoint. The company shared that it planned to stop further enrollment and shift focus to its only remaining trial, exploring the impact of ALRN-6924 on chemoprotection in p53-mutated breast cancer. With this announcement, Aileron's stock dropped by a drastic 41% in one day.

On October 11, 2022, Aileron officially terminated the trial on clinicaltrials.gov, specifically citing that they were unable to generate statistically significant results with the sample size of the trial.

The fallout: On February 21, 2023, Aileron announced the termination of the last trial for ALRN-6924, focused on p53-mutated breast cancer, sharing on clinicaltrials.gov a few days later that the first four patients enrolled experienced Grade 4 neutropenia and alopecia in their first cycle of treatment, failing both the primary endpoint and the main secondary endpoint.

This news sent the stock, which had been gradually falling since the news of the first trial's failure, an additional 38% in one day. This marked the official endgame for Aileron's sole drug candidate, prompting them to lay off most of the remaining staff and search for strategic options for an exit.

The bottom line: STAT Trials Pulse surfaced irregular signals that the ALRN-6924 trial may have been struggling for significance more than a year before

Aileron announced results that echoed these warnings. Staying on top of red flags in critical drug pipelines can aid investors in getting ahead of market-moving announcements and allow biopharma professionals to strategize ahead of time.

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Did irregular shifts in clinical trial progression at Flagship's Repertoire foreshadow the termination of its immuno-oncology program?

STAT Trials Pulse by AppliedXL detected red flags in the clinical activity for Flagship's portfolio company, Repertoire, over two years before terminations for both of their active pipelines were announced — terminations that ultimately led to a complete overhaul of the company's staff and focus..

Background: Repertoire Immune Medicines was born of Flagship Pioneering's 2019 merger of its two portfolio companies, Cogen Immune Medicines and Torque Therapeutics — marrying the foundational immune decoding and immuno-oncology platforms of each, respectively.

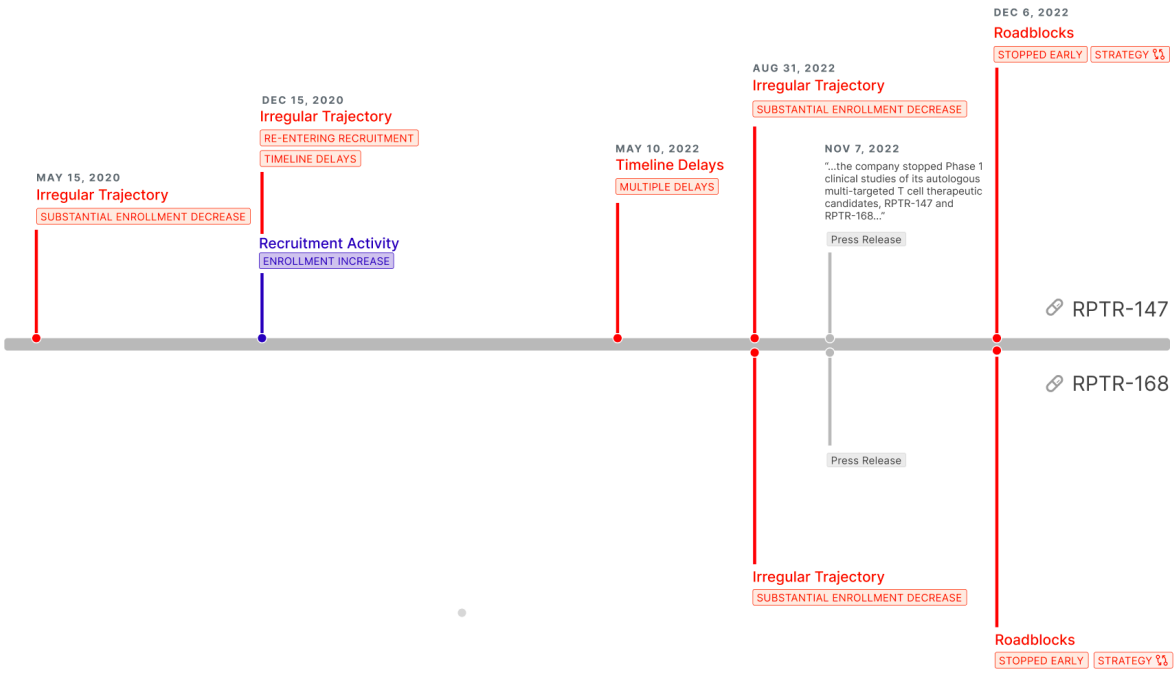
In April 2021, the newly-formed biotech raised $189M (in total, raising over $350M) to support its next stage of development and launched its first clinical phase candidate, RPTR-147. In February of 2021, a second candidate, RPTR-168, began clinical trials targeting HPV-16+ solid tumors.

Red flags: Irregularities began to surface in the RPTR-147's program on

May 15, 2020, when STAT Trials Pulse detected that the trial had closed recruitment with only 25% of its anticipated patients, enrolling 20 rather than the anticipated 80 patients.

Eight months later, on December 15, 2020, a new pre-news signal surfaced that the study had re-entered recruitment, simultaneously delaying its primary completion date by 17 months. At the same time, the study set a new enrollment target of 240 participants, an 11x increase from its actual enrollment of 20 patients. On May 10, 2022, the trial further delayed its projected primary completion date by more than three years, to July 2026.

On August 31, 2022, the RPTR-147 trial closed recruitment for a second time, only having enrolled 23 of its anticipated 240 patients. On the same day, STAT Trials Pulse detected an irregularity in Reportoire's other candidate study, the RPTR-168 trial targeting HPV-16+ tumors, as it closed recruitment with only 7 of its anticipated 24 patients.



The big picture: Substantial decreases in enrollment like those highlighted above are crucial early signals to note: falling substantially below enrollment targets may change the validity of initial trial design and efficacy assumptions. This can impact a trial's ability to achieve target power and statistically reliable results.

The impact: On November 7, 2022, Repertoire Immune Medicines officially announced that it would be discontinuing its two clinical programs, RPTR-147 and RPTR-168, specifying that the initial data showed little effect. On December 6, 2022, both trials were officially terminated on clinicaltrials.gov, citing the end of the development of the programs.

The fallout: The aftermath of these pipeline cuts was considerable, as Repertoire simultaneously announced the replacement of their CEO and layoffs for nearly half their staff. With no clinical pipeline currently in place, the remainder of Repertoire's post-overhaul staff has shifted focus on its DECODE platform, intending to identify novel therapeutic targets. Thus far, no new clinical activity has been initiated and the 'Programs' & 'Pipeline' sections of their site have been removed completely.

The bottom line: Irregularities in Repertoire's active pipelines signaled red flags over two years before their program termination was publicly announced, leading to a complete overhaul of the company's staff and focus.

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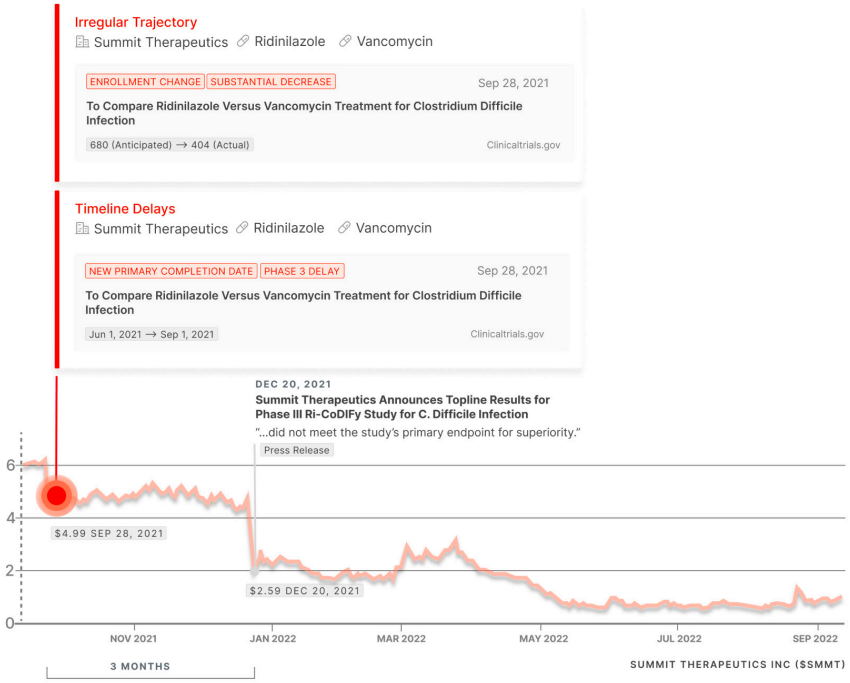
Could warning signs in Summit Therapeutics' clinical trial activity have hinted at bad results months before they were announced?

In late September of 2021, STAT Trials Pulse by AppliedXL surfaced irregularities in the trial progression of two pivotal studies in Summit Therapeutics' ridinilazole program, hinting at a problematic outlook for the program. 83 days later, the company publicly released results announcing that the primary endpoint was not met, fueling a sharp, same-day, 49% decline in the company's stock.

Background: Summit Therapeutics has been developing its lead drug candidate, *ridinilazole*, an investigational antibiotic targeting Clostridium difficile infection, for nearly 10 years. After a promising Phase 2 proof-of-concept study, two Phase 3 studies kicked off to assess the impact of the experimental drug compared to the commonly used antibiotic, *vancomycin*.

Red flags: In September 2021, compounding irregularities in its trial progression were detected by STAT Trials Pulse. These irregularities served as an early warning of potential problems within the program.



On September 28, 2021, both pivotal trials experienced delays and substantial drops in enrollment. Delays in Phase 3 trials are less common than in different stages of development, making up fewer than 9% of all clinical trial delays, and potentially affecting the timing of a drug's entry into market. Perhaps more concerning, falling substantially below enrollment goals may change the validity of assumptions around efficacy and study design, impacting a trial's ability to achieve target power and statistically reliable results. A majority of trials that experience this nature of enrollment change face roadblocks rather than complete according to regular trajectory.

These signals were detected and prioritized by STAT Trials Pulse's proprietary algorithm among thousands of other daily clerical updates on the NIH's public trial registry.

The impact: Nearly three months later, on December 20, 2021, a press release confirmed unfavorable results in the Phase 3 study, in which *ridinilazole* ultimately failed to outperform the common antibiotic *vancomycin*

with ample superiority. With this announcement, shares of Summit Therapeutics fell by a staggering 49%. Investors who had acted on these early signals could have avoided this fallout.

News buzz: As Summit Therapeutics' stock price nearly halved in the wake of the *ridinilazole* results, major news outlets such as Nasdaq began to provide commentary on the context behind the falling stock.

The fallout: *Ridinilazole* was Summit Therapeutics' main bet, and the only drug candidate for which they were conducting clinical-stage trials, leading its success (or lack thereof) to make a major impact on the market's perception of their prospects. At the time of publication, Summit's stock hovers just above a dollar. The company now clings to the possibility of a narrower approval among high-risk populations, although Merck's competitive and approved drug may edge this possibility out. Even with this potential, the revenue prospects for this indication are very limited compared to original projections.

The bottom line: Irregular activity for Summit Therapeutics' pivotal trials signaled red flags months before their unfavorable results were publicly announced. For competitive intelligence professionals and investors monitoring company pipelines, getting ahead of the curve can be a distinct advantage. STAT Trials Pulse detected and classified these nuanced irregularities 83 days before news broke, offering users potentially impactful insights.

To learn more about early signals like this, book a demo.

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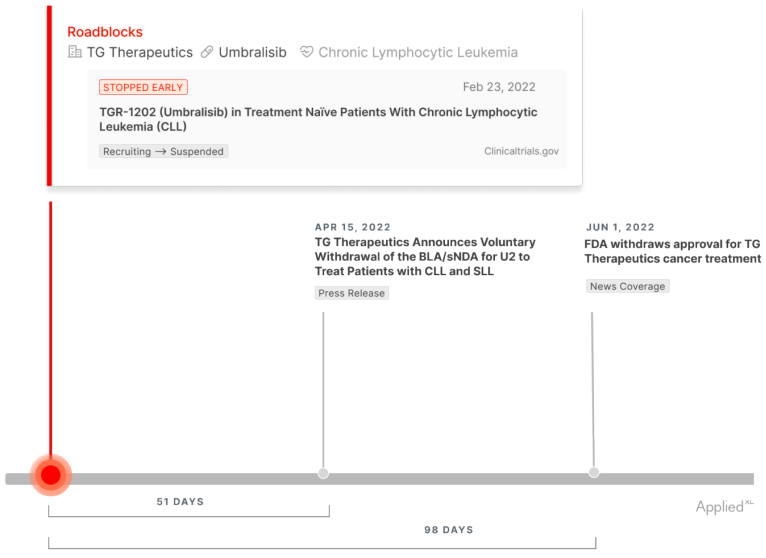
Could hidden signals in public data have anticipated bad news for TG Therapeutics $TGTX?

On Feb 23, 2022, STAT Trials Pulse by AppliedXL detected a clinical trial for TG Therapeutics' drug, umbralisib, unexpectedly stopping early due to safety issues — 51 days before the company publicly announced its voluntary withdrawal of umbralisib's drug application and the dissolution of its oncology program.

For biotech and pharma professionals as well as investors, getting ahead of the curve can be pivotal for taking strategic and timely action. Monitoring key changes hidden in public data sources can provide a distinct competitive advantage, as these may shed light on foundational signals that may otherwise go unnoticed.



Background: In February of 2021, TG Therapeutics received accelerated FDA approval for *umbralisib*, a kinase inhibitor targeting lymphoma. The FDA typically accelerates approvals of drugs that treat serious conditions and that fulfill an unmet medical need, based on a surrogate endpoint.

A hidden signal: A year later, what appeared to be a promising treatment candidate saw an unexpected setback. In February 2022, a TG Therapeutics-sponsored study was suspended *due to increased Serious Adverse Event (SAE) Occurrence*. The nature of this suspension is relatively rare, accounting for only about 2% of trials that stop early and signals serious disruptions to a drug's development. This consequential signal was detected and prioritized by STAT Trials Pulse's proprietary algorithm among thousands of other daily clerical updates on the NIH's public trial registry.

The impact: 51 days later, on April 15, 2022, TG Therapeutics announced the company would be voluntarily pulling *umbralisib* from the market, as well as withdrawing its application for use of this drug in other types of lymphoma. This decision was based on ongoing challenges with the drug's overall survival and safety data.

News buzz: On June 1, 2022 — 98 days after STAT Trials Pulse first detected the suspended trial — the *FDA officially* withdrew approval for TG Therapeutics' *umbralisib* cancer treatment due to a higher risk of death for patients receiving the drug. Major news outlets, including Reuters, began to report on the company's struggling drug development pipeline.

The fallout: The impact of this decision by the FDA led the company to terminate remaining trials in the *umbralisib* program, as well as halt enrollment in earlier stage oncology trials. The company is currently facing a class action lawsuit on behalf of people who purchased its stock, citing

a violation of the Securities Exchange Act — ultimately claiming that TG overstated the clinical and commercial prospects of its new drugs.

The bottom line: In this instance, the early indicator surfaced by STAT Trials Pulse in February could have provided a warning signal of the subsequent unraveling of the *umbralisib* program. For investors, biotech professionals, and competitive intelligence analysts in the pharmaceutical industry, time is often of the essence. With a 51-day head start, the ability to take early action before news broke could have provided a competitive advantage.

To learn more about early signals like this, book a demo.

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STAT trials pulse by Applied XL

Harnessing the Power of AI for Real-Time Clinical Intelligence in Biotech

The traditional process of obtaining clinical intelligence presents significant challenges for biotech executives, as it is slow, manual, and time-consuming. In an era where innovation in biological sciences is rapidly accelerating, staying informed is vital for effective decision-making and maintaining a competitive edge.

Professionals in this field have historically had to manually comb through vast amounts of published literature, trial databases, and other information sources to gain the necessary insights. This labor-intensive method not only consumes valuable time but also introduces the risk of human error, potentially leading to inaccuracies or incomplete understanding. The overwhelming volume of new data generated daily makes it increasingly challenging for biotech executives to track relevant developments and emerging trends. The need for a more efficient and reliable way of obtaining clinical intelligence has become increasingly apparent.

STAT Trials Pulse by AppliedXL now addresses this critical issue, empowering biotech executives to remain informed and agile in the ever-evolving world of biological sciences.

Imagine being alerted when multiple trials for a specific drug class are halted early due to efficacy concerns, when there is a sudden surge in a developing therapeutic

area, or even when patient demand increases for a certain therapeutic area. The STAT Trials Pulse platform developed in partnership with AI company AppliedXL is designed to meet these needs with an event-based approach to assess clinical activity.

The platform leverages machine learning to analyze publicly available data using algorithms that emulate journalists' research processes. It continuously tracks, categorizes, and contextualizes thousands of daily changes across various data sources, providing biotech professionals with the most relevant updates rather than a static view of the clinical landscape.

Real-time intelligence represents a significant advancement in monitoring clinical trials, one of the most expensive aspects of drug development. Currently, biotech companies have limited bandwidth to oversee emerging therapeutic areas tested in trial programs spread across numerous sites in countries worldwide.

Relevant signals surfaced by STAT Trials Pulse offer early insights into broader trends. The tool which is leveraged by global pharma companies, innovative biotech firms, and life sciences hedge funds, allows users to further refine topics, events, and trials, enabling them to analyze data more quickly and efficiently than ever before. It utilizes predictive algorithms to identify timeline delays, disruptions, and other problems well in advance so biotech professionals can be proactive in evaluating competitors as well as new growth and innovation opportunities.

The platform has already yielded significant results, detecting signals from clinical trials data before the information is publicly announced. A concept that AppliedXL calls "Pre-news".

The AI-driven classification of events streamlines the identification of patterns, anomalies, and outliers in the clinical domain. By continuously analyzing these data points over time, detection algorithms can reveal previously concealed trends in the clinical landscape.

Leveraging STAT Trials Pulse, biotech executives now have access to a unified database of clinical trials, empowering them to generate novel insights that were once difficult to acquire due to data silos.

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How STAT journalists used hidden signals in public data to unveil turmoil in one of the world's most valuable biotech startups

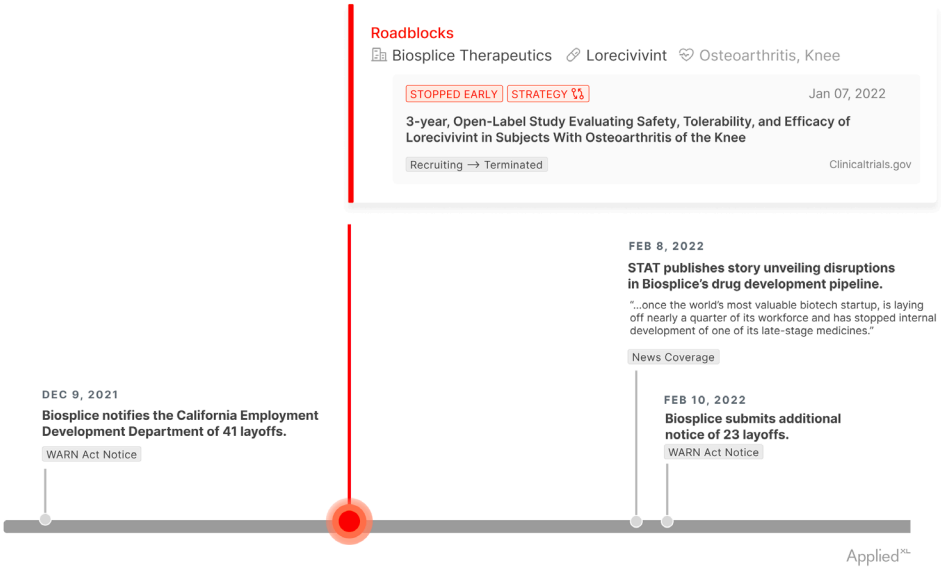
Data from STAT Trials Pulse by Applied XL helped identify disruptions that were hidden in plain sight, providing a more comprehensive look at the dysfunction in Biosplice's drug development pipeline.

Background: Entering the anti-aging field to much fanfare in 2016, Biosplice (then Samumed) was once the world's most valuable biotech startup. With an ambitious north star of targeting the biology of aging, the company aimed to treat the hallmarks of aging, such as arthritis, hair loss, and even cancer. In 2021, Biosplice's pipeline rested largely on *lorecivivint*, its treatment for osteoarthritis of the knee that was in Phase 3 trials, and *dalosirvat*, a drug in Phase 2/3 trials targeting androgenetic alopecia.

The hidden signal: On December 9, 2021, the company notified the California Employment Development Department of 41 layoffs, amounting to roughly a quarter of their staff. This notice caught the attention of Jonathan Wosen, STAT's West Coast biotech & life sciences reporter. Around the same

time, it became apparent that Biosplice had stopped internal development of *dalosirvat*, leaving all eyes (and future prospects) on the *lorecivivint* program.

Digging deeper, Wosen turned to STAT Trials Pulse to look under the hood of Biosplice's pipeline. It was there, on January 7, that he discovered that Biosplice had terminated a Phase 3 open-label study of *lorecivivint* citing "business reasons."



The impact: Having been in conversations with Biosplice around the company's broader situation, this surprising new insight allowed Wosen to ask the company questions he otherwise wouldn't have. "I don't think the company would have told us they stopped this open-label trial [if we hadn't discovered the event on STAT Trials Pulse]. This was the kind of thing we had to come to them with and ask them to provide an explanation for, on the record, " he remarked, when asked of the impact of this signal.

News buzz: On February 8, 2022, STAT published a story co-authored by

Wosen and STAT's Matthew Herper, which laid out the full gamut of issues that Biosplice was facing – from *dalosirvat* to *lorecivivint*. While other outlets later reported on the Biosplice layoffs as well, STAT was the first source to provide a sweeping context of the company's situation. While the news buzz referenced that the future of the company rested now, largely, on the *lorecivivint* program, only STAT coverage provided the pivotal context that *lorecivivint*, too, was facing problems.

Further impact: Two days after the story was published, on February 10, Biosplice filed a second notice with the California Employment Development Department regarding an additional layoff of 23 employees.

The bottom line: In the age of big data, journalists must find innovative ways to analyze and find stories in large datasets. STAT reporters used STAT Trials Pulse to do just that. By digging beyond what the company was communicating publicly, they were able to unveil the full story.

These cutting-edge approaches to gathering information are now available to professionals across the life sciences industry. Book a demo to learn more!

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How Feldan Therapeutics uses "kill sheets" to make data driven decisions about clinical development

Navigating information overload effectively

Feldan Therapeutics is a biopharmaceutical company that specializes in developing treatments based on the intracellular delivery of therapeutics. Put simply, the company has developed a proprietary technology that enables the safe and efficient delivery of various therapeutics inside cells. By giving access to intracellular components beyond the reach of existing treatments, Feldan's technology is creating new opportunities in drug development.

In a highly dynamic and specialized market, VP of Finance & Business Development Vincent Ménard and Strategic Development Project Manager Jean-Pascal (JP) Lepetit-Stoffaes are responsible for the monitoring of new growth opportunities. Data plays a crucial role in informing their decisions, but often there's too much of it. To filter out unimportant updates and find the right insights, Feldan's business team has turned to STAT Trials Pulse by Applied XL.

Less time searching for data means more time to make decisions

Historically, the process of scanning the clinical trials landscape for new data and insights has been mostly manual at Feldan. Having access to a tool like STAT Trials Pulse by AppliedXL, which allows new clinical trial data to be continuously updated across multiple sources, was therefore a game-changer for the small company. Ménard and Lepetit-Stoffaes realized that they could accelerate their data-gathering process by leveraging this new tool, allowing them to operate strategically.

"As a small biopharmaceutical company, we don't have all the resources of a large company. We must be agile in the way we work," explained Ménard.

Staying on top of the latest clinical trial information allows the Canadian company to create internal strategic alignment, to accelerate decision-making and to better articulate its positioning to investors.

"It's crucial to have a platform that allows us to save time by not having to go through multiple websites to build our analysis. That's why STAT Trials Pulse is very useful to us: It makes our daily work easier and more efficient," said Lepetit-Stoffaes.

Using datat to know what project to kill early

Accessing data is one thing; analyzing it effectively is another. With new data now at their fingertips, Feldan's business team developed a core evaluation approach to identify which projects to pursue, and which ones to drop. The so-called kill sheet provides a framework that helps the team assess the scientific validity, competitive landscape, market size, and clinical feasibility of projects under evaluation. This analysis guides whether the company should

proceed with a specific project and thus spend valuable resources on preclinical development and clinical trials, or stop it.

"We need to make sure we are spending the right amount of time evaluating projects. Since we cannot work on multiple things at once, we need to quickly and efficiently identify the projects that turn out to have little potential and "kill" them. That way, we can focus on the ones that have the most chance of working in the long run," said Ménard.

COURTESY OF FELDAN THERAPEUTICS

In addition to helping Feldan's team to streamline their project pipeline, STAT Trials Pulse by AppliedXL also allows them to collect strategic context around status changes, and monitor roadblocks that other sponsors encounter. By setting up automated monitoring of comparable studies, Ménard and Lepetit-Stoffaes have been able to evaluate potential challenges to their own projects."When our competitors interrupt their trials, we need to understand whether it could stem

from drug availability issues, or target issues. In this former situation, we can show an edge by proposing a technology that may deliver the drug more efficiently," they explained. With its smart filters and event detection platform, STAT Trials Pulse by AppliedXL is saving the team valuable time in the research process, allowing Feldan Therapeutics to assess their opportunities faster and continue to innovate.

Book a demo today to learn more about STAT Trials Pulse by AppliedXL.

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About STAT Trials Pulse

STAT and AppliedXL have partnered to bring you STAT Trials Pulse. AppliedXL brings to the table an experienced team of computational journalists and engineers who specialize in real-time information processing. STAT builds on its track record of deep reporting on health and medicine, to inform AppliedXL's clinical trials algorithm. By combining the precision of data science with the high standards of journalism, we've unlocked a powerful new way to surface the most relevant updates in the clinical trials space.

About AppliedXL

AppliedXL is a real-time information company combining machine learning techniques with the principles of investigative journalism. Its technology is used to power STAT Trials Pulse, a platform that enables biotech and pharma professionals to make faster decisions with the help of real-time alerts, dashboards, and briefings. We believe in holding data to a higher standard by representing information with focus and clarity, while also finding meaning with human context.

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