FDA Rejects Petition for Review of Gene Therapy Product for Safety Concerns Involving Vulnerable Patient Population

https://www.trialsitenews.com/a/fda-rejects-petition-for-review-of-gene-therapy-product-for-safety-concerns-involving-vulnerable-patient-population-dc2cb736

TSN

TrialSite Staff

Staff at TrialSite | Quality Journalism

Sep. 1, 2022, 5:00 p.m.

Is the filing of a citizen petition with the U.S. Food and Drug Administration (FDA) an appropriate action for requesting review of a Biological License Application (BLA) if there are safety concerns in a particular gene therapy involving vulnerable patients? Apparently not, according to a letter from Peter Marks, Director of the agency's Center for Biologics Evaluation and Research Director to Patrick Girondi, founder, and Chief Executive Officer of San Rocco Therapeutics LLC (SRT).

Founded by Patrick Girondi—featured in *TrialSite's* "Family Man" series about a man who came from the rough and tumble streets of South Chicago who dropped his successful career in commodity trading to find a cure for his son struck with thalassemia. SRT not only competes against bluebird bio, but also according to a recent interview with *TrialSite's* founder Daniel O'Connor, SRT has developed a superior gene therapy for the target vulnerable patient population: one that is safer and far more economical. The bluebird gene therapy Zynteglo will cost over $2.8 million with the SRT gene therapy coming in at a forecasted $700,000. SRT must play serious catch up however, as Zynteglo has been granted a BLT while SRT must still enter Phase 1 clinical trials.

The FDA rejects the petition to review the BLA for the gene therapy Zynteglo (betibeglogene autotemcel) despite the ongoing patent dispute between San Rocco and bluebird and the fact that the bluebird gene therapy

lacks an insulator, an advanced feature that according to Girondi, San Rocco's license with Memorial Sloan Kettering includes.

San Rocco used this not well understood FDA process to halt the approval of the bluebird gene therapy so that the regulator can conduct a "careful investigation" of the biologics license application for betibeglogene autotemcel (beti-cel) and withhold final approval until the resolution of San Rocco's patent infringement suit against bluebird. Girondi told *TrialSite,* "The Citizen petition was embraced as a rational means to ensure a meaningful review of the BLA in terms of safety and risks could be accomplished."

But the FDA's Marks noted in the rejection letter to Girondi and San Rocco that a citizen petition is not appropriate for requesting review of a BLA, sharing that the petition "does not contain facts demonstrating any reasonable grounds for the requested actions."

He said citizen petitions can request that FDA issue, amend, or revoke a regulation or an FDA order, or take or refrain from taking an administrative action, and are to be resolved based on information in the administrative record.

Marks went on the record in this response to San Rocco: "An investigation is not an administrative action, and, as the Petition implicitly acknowledges, investigations necessarily require fact finding beyond what is presented in the current administrative record."

Approved in Summer of 2022

As reported by the *Pinksheet* earlier this summer, the FDA's Cellular, Tissue, and Gene Therapies Advisory (CTGTA) Committee voted unanimously that the product's (Zynteglo) benefits outweigh its risks in the target population.

Members of the CTGTA declared the therapy's "impressive efficacy" and "minimal risk" make it possibly a game changer treatment in the treatment of transfusion-dependent beta-thalassemia, a type of inherited blood disorder.

San Rocco's request is distinct from typical petitions asking the agency to require sponsors of abbreviated new drug applications to submit additional information.

The agency had a similar response to a citizen petition used by investors involving Cassava Sciences, Inc.

TrialSite reported that last year, Jordan Thomas, a partner at Labaton Sucharow, requested that the agency halt two ongoing trials of Cassava's investigational Alzheimer's disease treatment Simufilam pending a thorough audit by the agency. In a February 22nd letter denying the petition, the Center for Drug Evaluation and Research Director Patrizia Cavazzoni used the same language as Marks. She said the petition was requesting FDA to initiate an investigation and that an investigation is not an administrative action.

The Competition—Comparing Vectors

Based in Tampa, Fla., SRT was previously Errant Gene Therapeutics, LLC. The privately held company announced its name change in May 2021, noting that San Rocco is the patron saint of hopeless disease.

As *TrialSite* reported in the "Family Man" series, Errant was founded in 1993 after Girondi's son was diagnosed with thalassemia. The company's website says the lead compound for its cell and gene therapy platform, enhanced TNS9 for treatment of thalassemia, will soon enter Phase I clinical trials.

SRT describes itself in relation to bluebird. In an April 12th release about a Memorial Sloan Kettering study using SRT's vector, SRT said patients treated with bluebird's vector have had issues with clonal dominance, myelodysplastic syndrome, and leukemia. It included a tweet about FDA's December 2021 partial hold on bluebird's gene therapy for sickle cell disease along with a button to retweet. (Also see "Safety Concerns Hit Bluebird Sickle Cell Trial, Again" - Scrip, 20 Dec 2021.)

The citizen petition also cites the FDA's past suspensions of bluebird studies. It contends that SRT's vector is safer. In 2017, SRT sued bluebird and Sloan Kettering Institute for Cancer Research (SKI) in the Supreme Court of New York alleging that SKI disclosed its confidential information to bluebird. The parties reached a confidential settlement agreement during the trial in November 2020.

The 'Family Man's' Continued Struggle Against 'Capitalist Machine'

SRT filed a patent infringement suit against bluebird and Third Rock Ventures in October 2021 in the US District Court for the District of Delaware. US District Judge Richard Andrews issued an order on July 28th staying the case pending the results of arbitration.

In a July 26th memorandum, he noted that in a 2005 exclusive license agreement, Memorial Sloan Kettering through its affiliate SKI granted SRT an exclusive worldwide right and license to commercially develop a drug practicing the two patents-in-suit.

The agreement was terminated in 2011. Judge Andrews said the 2020 agreement settling the New York litigation and a separate suit against Third Rock includes a license provision that MSK shall give SRT an exclusive, royalty-free commercial license to the intellectual property licensed in the 2005 agreement and any intellectual property for which developing, using, or selling "the TNS9.3.55 vector or any modified or related lentiviral vector would be or could be infringed." He noted that the parties have opposing interpretations of the grant of an "exclusive, royalty-free commercial license" and the scope of the release provision in the 2020 agreement.

As for SRT's request that FDA hold off on licensing Zynteglo until the patent dispute is resolved, Marks said the petition did not provide adequate legal grounds to do so. The Public Health Service Act "generally does not contemplate any involvement by FDA in patent-related matters in the context of a BLA (such as the beti-cel BLA) submitted under section 351(a) of the PHS Act," Marks stated.

The petition also criticized bluebird's "exorbitant price" for Zynteglo. Bluebird announced a list price of $2.8m for the one-time treatment and said it is negotiating outcomes-based agreements with payers in which bluebird will reimburse up to 80% of Zynteglo's cost if a patient fails to achieve transfusion independence within a defined period. (Also see "Bluebird's Zynteglo Approval Kicks Off Commercial Operations" - Scrip, 17 Aug 2022.) SRT said it aims for a one-time price of $700,000 for its therapy.

FDA
Gene Therapy
Investors
Safety