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US FDA Quashes Citizen Petition Against Bluebird's Zynteglo That Cited Patent, Safety Concerns

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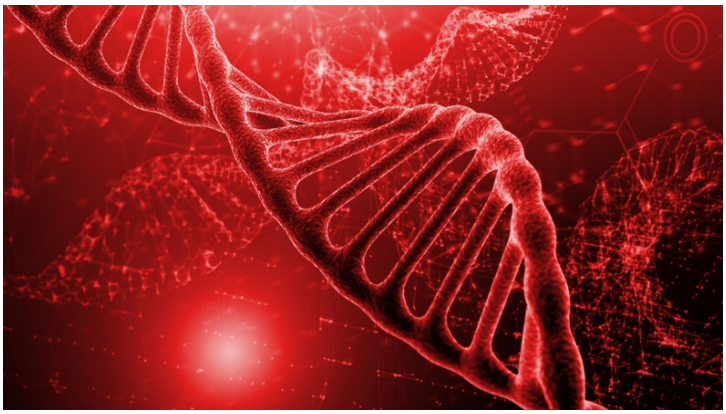
Executive Summary

San Rocco, whose potential rival gene therapy for thalassemia is in preclinical development, had wanted FDA to delay approval of bluebird's BLA until resolution of a patent case and a 'careful investigation' of Zynteglo's risks.



FDA REJECTS PETITION SEEKING TO DELAY APPROVAL OF BLUEBIRD BIO'S BLOOD DISORDER GENE THERAPY

Source: Shutterstock

The small biopharma company San Rocco Therapeutics, LLC struck out in its attempt to delay approval of bluebird bio's Zynteglo (betibeglogene autotemcel) for the treatment of beta-thalassemia through an unusual citizen petition.

The company requested the US Food and Drug Administration to 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. The agency denied the citizen petition on 17 August, the day it approved Zynteglo.

In a letter to San Rocco founder Patrick Girondi, Center for Biologics Evaluation and Research Director Peter Marks said the petition "does not contain facts demonstrating any reasonable grounds for the requested actions."

Marks noted that a citizen petition is not appropriate for requesting review of a BLA. He said citizen petitions can request that FDA issue, amend, or revoke a regulation or an

order, or take or refrain from taking an administrative action, and are to be resolved based on information in the administrative record.

“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,” Marks stated.

He noted that FDA conducted a thorough review of bluebird’s BLA to determine if it met the requirements for licensure, including a demonstration that the product is safe, pure, and potent. The agency approved Zynteglo, a one-time gene therapy, for adult and pediatric patients with beta-thalassemia who require red blood cell transfusions. The agency noted that there is a potential risk of blood cancer associated with the treatment but said no cases were seen in studies of Zynteglo. (Also see "Keeping Track: Axsome’s Auvelity Survives Long Review; Bluebird’s Zynteglo Cleared For Liftoff; Omeros Appeals CRL" - Pink Sheet, 19 Aug, 2022.)

The FDA’s Cellular, Tissue and Gene Therapies Advisory Committee voted unanimously that the product’s benefits outweigh its risks in the target population. Members said the therapy’s “impressive efficacy” and “minimal risk” make it a potential game-changer in the treatment of transfusion-dependent beta-thalassemia, a type of inherited blood disorder. (Also see "Gene Therapy: Bluebird’s Beti-Cel Sails Through US Panel Review On Strength of ‘Impressive’ Efficacy" - Pink Sheet, 10 Jun, 2022.)

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 involving brand company Cassava Sciences, Inc. 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. (Also see "Cassava Dives Again After Investors Spooked By Alzheimer’s Drug Fraud Claims" - Scrip, 27 Aug, 2021.)

In a 22 February letter denying the petition, 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.

Comparing Vectors

Based in Tampa, Fla., San Rocco Therapeutics (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. 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 a 12 April 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.

Memorial Sloan Kettering Licensing Agreements

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 28 July staying the case pending the results of arbitration.

In a 26 July 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.