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Duo Falter Again On US Belbuca ANDA, Eight Years After Joining Hands

Second CRL Demands More Quality Information; Questions Swirl Around Teva Appetite

by Dean Rudge

IntelGenx has once again been frustrated in its attempts to challenge Collegium's powerful opioid Belbuca in the US, amid ongoing litigation over the brand's three US patents that run until December 2032. Meanwhile, Teva's desire to push on with its own January 2027 launch has been called into question.

IntelGenx Technologies must provide the US Food and Drug Administration with additional pharmaceutical quality information for an abbreviated new drug application referencing Collegium's Belbuca (buprenorphine) buccal film, according to a complete response letter denying approval once again for the proposed generic in its current form.

"The FDA confirmed that no additional inspection of IntelGenx's facility is required at this time," the oral film specialist clarified, after the potential for such an inspection threatened to push the GDUFA date for the ANDA into July 2024.

IntelGenx partnered on the proposed Belbuca generic with Insud Pharma's Chemo group and its US-based affiliate Xiromed almost eight years ago, in September 2016. It underlined that Xiromed was "committed to providing the FDA with a response to the CRL as soon as is practicable."

It's the second CRL received by Xiromed in less than a year. In late April 2023, after being knocked back, Xiromed and IntelGenx said that they would contact the FDA to discuss the initial CRL and "assess the filing of a request for reconsideration."

Xiromed had then submitted to the FDA an amendment to the ANDA, requesting priority review. This was granted by the agency, providing an eventual goal date for review of the amendment of 8 March, which overran by several weeks.

“I don’t really know what the issues are,” admitted IntelGenx’s CEO, Dwight Goram, speaking to investors last month as Xiromed awaited word from the FDA. “It’s really between Xiromed and the FDA, and as soon as they know, they’ll let us know.”

Meanwhile, IntelGenx had acknowledged that it would likely run out of capacity “sometime in 2025 or 2026” as it looked to manufacture sufficient quantities of its proposed Belbuca generic, leading the firm to once again look to raise funds to invest in infrastructure.

“That would probably not be funded through equity. We’re looking at different scenarios, maybe a bank loan, government support, maybe a partner in support. Most likely, we wouldn’t have to raise equity, but that’s where we think we are at this point.”

“But it will depend obviously on the launch date and the numbers that we’ve been told. If they meet those numbers, we might be facing that [raising funds] sooner than later.”

Teva Appears Neutral As Launch Date Approaches

The proposed generic buprenorphine buccal film product, a powerful opioid for severe, around-the-clock pain, incorporates IntelGenx’s proprietary VersaFilm technology in a novel formulation, designed to be a bioequivalent, lower-cost alternative for patients.

Approved by the FDA in October 2015, Belbuca enjoys protection from two drug product patents until July 2027, with a further US patent potentially extending its monopoly until December 2032.

IntelGenx, Insud, Chemo and Xiromed have together been sued for patent infringement by Collegium’s BioDelivery Sciences affiliate in a US district court in Delaware. The originator alleges infringement of all three patents, seeking a declaratory judgment of patent infringement. The case is ongoing, with no trial date yet determined.

In a recent expansive note, Jefferies acknowledged Teva’s February 2018 patent-litigation settlement agreement which allows it to launch a Belbuca generic in January 2027.

However, the analyst noted: “Based on Teva's clear strategic pivot away from generics and towards innovative medicine coupled with the $4bn+ opioid settlement, we would not be surprised if Teva decides not to move forward with generic opioid drugs.” (Also see "*Teva Wraps Up Nationwide US Opioids Settlement*" - Generics Bulletin, 9 Jun, 2023.)

Teva has yet to receive tentative approval for its proposed Belbuca generic and has relinquished first-to-file status, Jefferies noted, strengthening its case against the firm by observing that the company was also looking hesitant on its approach to another of Collegium's opioids, Nucynta (tapentadol) extended-release tablets.

"Teva is one of two companies that settled on Nucynta ER [for market entry] in 2026. But based on our conversations with Collegium's management, tapentadol active pharmaceutical ingredient is not readily available, must be made in the US, and takes two or three years for a drug master file to scale the drug, which we would expect should be ongoing if the company planned on launching in 2026," Jefferies explained.

Meanwhile, according to Jefferies, Collegium did not think Teva had so far secured an authorized generic partner "and hasn't seen signs of scaling manufacturing."

"At a minimum, this seems to indicate Teva's current plans for a generic Nucynta ER are unclear," Jefferies noted. "With that said, if Teva does not develop a generic Nucynta ER for 2026, we think it increases the likelihood they do not develop a generic Belbuca for 2027."

This would be a "meaningful catalyst for Collegium as it would result in five additional years of exclusivity," considering another ANDA filer, Alvotech, has settled on a launch for 2032.