

Durata's Dalbavancin Hits the Home Stretch

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With a new road map in hand, Durata Therapeutics Inc. has its lead candidate, dalbavancin, back on course for what it hopes is the final lap to FDA approval for the treatment of acute bacterial skin and skin structure infections (ABSSSI).

The long-acting, intravenous lipoglycopeptide is being evaluated in a global, pivotal, Phase III study conducted under a special protocol assessment (SPA) that reflects the FDA's most recent draft guidance on developing ABSSSI drugs.

Durata expects to enroll about 556 patients worldwide in the DISCOVER-1 trial comparing the efficacy and safety of dalbavancin to vancomycin. The primary endpoint will be the cessation of the spread of infected lesions and an absence of fever at 48 to 72 hours following initiation of treatment.

The Morristown, N.J.-based company hopes to file for FDA approval by the first quarter of 2013, CEO Paul Edick told *BioWorld Today*.

It won't be the first time dalbavancin has come up for approval. Once owned by Pfizer Inc., of New York, dalbavancin's initial route to market hit a detour when the FDA changed its thinking on noninferiority trials and how ABSSSI drugs should be developed.

Although the drug met its primary endpoint for the treatment of complicated skin infections, including those caused by methicillin-resistant *Staphylococcus aureus* (MRSA), in a Phase III noninferiority study that enrolled more than 800 subjects, the drug was handed an approvable letter in 2007. (See *BioWorld Today*, Dec. 23, 2009.)

At that time, Pfizer said the FDA, which had recently published draft guidance on noninferiority studies as the basis for approval of antibacterial products, had requested additional data.

Recognizing the potential of dalbavancin, a venture capital syndicate formed Durata in 2009 to bring the drug to market. "We formed the company around this," Edick said.

Durata recently acquired the Japanese rights to the antibiotic from RaQualia Pharma Inc., of Aichi, Japan, giving the start-up "unencumbered global rights," Edick said. RaQualia received an undisclosed up-front payment and the promise of development milestones and royalties on sales in Japan.

Durata hopes to get sufficient Japanese sites in the DISCOVER-1 trial to support marketing approval in that country, Michael Dunne, the company's chief medical officer, told *BioWorld Today*.

While Durata's attention is focused on getting to the finish line with the development of dalbavancin, Edick said, "All options are on the table" when it comes time to commercialize the drug.

Although the company was set up to develop late-stage candidates, it could commercialize the antibiotic if that appears to be the best strategy.

If dalbavancin is approved, it could have some stiff competition, most of which also was stalled when the FDA started second-guessing its position on noninferiority and ABSSSI trials. The trouble began in 2006, when the agency rejected Replidyne Inc.'s new drug application for the antibiotic faropenem, calling for superiority trials even though noninferiority had been good enough in the past. (See *BioWorld Today*, Sept. 13, 2006.)

From there, things went from bad to worse, as telavancin (Theravance Inc.), oritavancin (Targanta Therapeutics Corp.), ceftobiprole (Basilea Pharmaceutica AG), iclaprim (Arpida AG) and cethromycin (Advanced Life Sciences Inc.) all failed to gain a first-pass approval.

South San Francisco-based Theravance Inc. and partner AstraZeneca plc, of London, finally won approval for Vibativ (telavancin) in 2009, nearly three years after first submitting its new drug application for the ABSSSI indication. (See *BioWorld Today*, Sept. 15, 2009.)

Before shifting back into gear, a number of companies with ABSSSI candidates, including Durata, decided to wait for guidance, Edick said.

Trius Therapeutics Inc., of San Diego, was one of the first back on track. Its SPA for the first of two planned Phase III trials for torezolid in ABSSSI was based on the FDA's draft guidance on noninferiority trials released in March 2010. (See *BioWorld Today*, June 17, 2010.)

The trial, comparing torezolid with Pfizer's Zyvox (linezolid), was set to begin in the second half of 2010, delivering top-line data in early 2012. The FDA's draft guidance on ABSSSI, the first in 12 years, wasn't released until last August.

As the next generation of oxazolidinone antibiotics, torezolid is intended to improve on Zyvox, which generated \$1.1 billion in 2009.

Despite the competition, Durata is confident about dalbavancin's position. "Due to its unique features and PK profile, dalbavancin offers the significant convenience of once-a-week dosing and short, 30-minute infusion time," Dunne said, adding that the antibiotic "has the potential to set the bar for activity against important Gram-positive bacterial infections, including those due to MRSA."

Meanwhile, the FDA signaled in its draft guidance there could be more changes down the road for the development of ABSSSI antibiotics.

Noting ongoing efforts in the scientific community regarding trial designs and endpoints for ABSSSI, the agency said it expects to revise the guidance as the "science of clinical trial design for this indication evolves."