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Interchangeable would be game changer for Humira competition

By Mari Serebrov, Regulatory Editor

A double-header this week in which the FDA's Arthritis Advisory Committee (AAC) will be looking at potential biosimilars for two more TNF-inhibitors is creating a lot of buzz about when biosimilar competition for Humira and Enbrel will hit the U.S. market.

But one company is already pushing past biosimilars, hoping to score big with a Humira (adalimumab, Abbvie Inc.) interchangeable. In lieu of FDA guidance on interchangeability, Oncobiologics Inc., of Cranbury, N.J., has been working with the regulator on trial protocols to demonstrate its follow-on is both biosimilar to and interchangeable with Abbvie's blockbuster biologic.

Recognizing that "Humira is a crowded landscape" for biosimilars, Oncobiologics Chairman, CEO and President Pankaj Mohan told *BioWorld Today* his company plans to be in the first innings of competition with its interchangeable.

"Interchangeability would change the game for Humira," Mohan said. It also would be a game-changer for biosimilars hoping to compete in the space, as it could give the interchangeable the advantage of automatic substitution, which could lead to a price discount much lower than the 15 percent to 30 percent offered by biosimilars.

To get its lead product to home plate, Oncobiologics is following a combined biosimilar-interchangeability strategy utilizing an integrated phase III program with two protocols and the same plaque psoriasis patient population. The first protocol is designed to demonstrate biosimilarity, while the second aims at showing interchangeability. Together, the two protocols should take one year.

The Biologic Price Competition and Innovation Act (BPCIA) set the bar much higher for an interchangeable. Whereas biosimilars in the U.S. must be "highly similar" to the reference product, interchangeables must produce the same clinical results as their reference drug in any given patient. The risk, in terms of safety or diminished efficacy, of switching between an interchangeable and reference biologic must not be greater than from consistent use of the reference product.

Given the higher bar and the FDA's delay in releasing guidance on interchangeability, most companies have focused on biosimilarity. The conventional wisdom is that they can demonstrate interchangeability later.

However, in addition to the competitive advantage of automatic substitution, the BPCIA offers a reward for being the first U.S. interchangeable referencing a specific innovator – market exclusivity.

DEVELOPING AN INTERCHANGEABLE

So how does a pure-play start up like Oncobiologics swing for a grand slam when the FDA hasn't pitched interchangeability yet? Mohan said the company sought out the agency's advice and has been working closely with FDA staff to design its phase III trial.

The protocol Oncobiologics recently got approved calls for multiple switches from the innovator to the follow-on and vice versa, Mohan said, and is quite different from a biosimilar study that generally requires one switch from the reference product to the biosimilar candidate after the primary endpoint has been met.

In light of his interaction with the FDA, Mohan said it wouldn't be possible to deem a follow-on as interchangeable based on biosimilarity studies.

Oncobiologics plans to file an IND with the FDA for its Humira follow-on this year and hopes to launch its flagship product in 2018 or 2019 as part of the first wave of competition. Whether it pursues a biosimilar label first or goes straight for interchangeability in the U.S. will depend on patent issues.

"We have navigated around this landmine," Mohan said of Abbvie's formulation patent. But the North Chicago-based innovator has protected its $14 billion drug with a thick patent fence.

That could present problems not just for Oncobiologics but for other companies with follow-ons in the works. Amgen Inc., of Thousand Oaks, Calif., is presenting its ABP-501 as a Humira biosimilar to the AAC Tuesday. Although the FDA seems to be favorably disposed toward approving the drug, Credit Suisse analyst Vamil Divan said in a research report last week that Abbvie's patents could prevent Humira biosimilars from entering the U.S. market until 2021.

Oncobiologics isn't just focused on the U.S., though. The

company is following the voluntary harmonization procedure and has approval to begin clinical trials for its Humira biosimilar in several EU countries. It plans to start enrolling patients in those trials, as well as in Canada, within the next three months. Mohan said Oncobiologics had looked to the U.K. as an anchor to the drug's EU development. It's too soon to say whether Brexit will change those plans.

ENBREL BIOSIMILARS

The AAC's second meeting this week will home in on Sandoz Inc.'s GP2015, developed as a biosimilar to Amgen's Enbrel (etanercept). As with Amgen's biosimilar application, the FDA voiced support for the Sandoz drug. Again, patents could keep an Enbrel follow-on off the U.S. market for several more years. The FDA licensed Enbrel in 1998, but a U.S. patent extension could protect the biologic for 12 more years.

Meanwhile, the EMA approved the EU's first Enbrel biosimilar in January, giving the nod to Samsung Bioepis Co. Ltd.'s Benepali, which was launched last year in South Korea as Brenzys. (See *BioWorld Today*, Jan. 20, 2016.)

Although their U.S. launch could be delayed by patents, the Amgen and Sandoz candidates are positioned to be the second and third FDA-approved biosimilars to TNF-inhibitors. In April, the agency approved Celltrion Inc.'s biosimilar to another TNF-blocker, Janssen Biotech Inc.'s Remicade (infliximab). That follow-on will be marketed by Pfizer Inc. in the U.S. as Inflectra. (See *BioWorld Today*, April 13, 2016.)