GENERICS BULLETIN
CITELINE COMMERCIAL

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Alvotech Makes Multiple Moves As It Allies With Advanz For Five European Biosimilars

Firm Also Drops Products From Stada Deal And Reveals A Pair Of New Pipeline Products

by David Wallace

In a busy week for Alvotech, the firm has announced an expansion of its partnership with Advanz to cover five further European biosimilars, at the same time as revealing two new pipeline assets. Meanwhile, the company has also dropped three products from an existing European partnership with Stada and has also terminated a development deal with BiosanaPharma.

Alvotech has announced a five-product biosimilar commercialization deal with *Advanz Pharma* in Europe, capping a busy week that has also seen the biosimilars developer make a number of other key disclosures relating to its pipeline and partnerships.

One of these involved revealing biosimilar Entyvio (vedolizumab) and Keytruda (pembrolizumab) candidates as part of its pipeline, while Alvotech has also dropped three products from its existing deal with *Stada* and has terminated a co-development licensing deal with *BiosanaPharma* on a proposed biosimilar to Xolair (omalizumab).

Key Takeaways

- Alvotech and Advanz have partnered to commercialize five proposed biosimilars in Europe
- Alvotech has also just disclosed Entyvio (vedolizumab) and Keytruda (pembrolizumab) biosimilar candidates in its pipeline
- The Advanz deal includes biosimilars to Simponi (golimumab), Entyvio

Announcing the deal with Advanz – which builds on a partnership from earlier this year that gave Advanz exclusive rights to Alvotech's Xolair (omalizumab) biosimilar in various global markets (Also see "*Advanz Agrees Multi-Market Omalizumab Deal With Alvotech*" - Generics Bulletin, 6 Feb, 2023.) – Alvotech said the agreement would include its AVT05 proposed biosimilar to Simponi (golimumab) and AVT16 Entyvio rival, along with three other undisclosed early-stage biosimilar candidates, and would cover the European Economic Area, the UK and Switzerland.

According to IQVIA data, the five biosimilars together have a current addressable market of more than $4bn in the territories covered by the deal.

(vedolizumab) and three additional undisclosed products

- Alvotech and Stada have dropped the Simponi (golimumab) and Entyvio (vedolizumab) biosimilars as well as a Prolia/Xgeva (denosumab) rival from their partnership
- Alvotech has also announced the termination of a co-development deal with BiosanaPharma for a biosimilar Xolair (omalizumab) candidate
- Alvotech also provided the latest update on progress towards obtaining US FDA approval for its Humira (adalimumab) biosimilar

"Advanz Pharma will leverage its existing specialty and hospital capabilities in Europe to ensure successful market registration, commercialization, and patient access," Alvotech indicated. Alvotech will be responsible for development and commercial supply while Advanz handles registration and commercialization.

Advanz "will make upfront payments in the aggregate amount of €56.0m ($60.1m) at signing of the product schedules," Alvotech said, "and agreed to make additional payments for an aggregate amount of up to €264m upon the achievement of certain development and commercial milestones." Advanz will buy the biosimilars "at a royalty of approximately 40% of the estimated net selling price or an agreed-upon applicable floor price, whichever is higher, for the duration of the relevant product schedule."

"We are very excited to extend our existing partnership with Advanz Pharma into additional therapeutic areas," said Alvotech chairman and CEO Robert Wessman. Alvotech chief commercial officer Anil Okay added that "after signing our initial partnership agreement with Advanz earlier this year, we look forward to deepening our relationship and working with Advanz on bringing additional important therapies to market in Europe."

Meanwhile, Advanz CEO Steffen Wagner – who previously served as head of Europe for Stada, with which Alvotech has a longstanding European biosimilars alliance (Also see "*Advanz Appoints*

Stada Europe Head As New CEO" - Generics Bulletin, 19 Nov, 2021.) – said the partnership "positions Advanz Pharma as a key future player in European biosimilars" while also serving as "an important next step in Advanz's ambition to be a partner of choice for the commercialization of specialty, hospital, and rare disease medicines in Europe."

And Advanz chief corporate development officer Susanna El-Armale reiterated that the partnership "materially strengthens Advanz's pipeline of specialty pharmaceuticals to drive mid- and long-term sustainable growth."

Alvotech Drops Three Products From Stada Alliance…

This week has also seen Alvotech announce three termination agreements with Stada that bring to an end licensing and supply partnerships on three biosimilars: Alvotech's AVT03 proposed rival to Prolia/Xgeva (denosumab) – a candidate that entered clinical trials nearly a year ago and is not part of the Advanz alliance (Also see "*Alvotech Makes It Four With Denosumab Trial*" - Generics Bulletin, 22 Jul, 2022.) – as well as the AVT05 golimumab and AVT16 vedolizumab products covered by the Advanz deal.

"Pursuant to the terms of the termination agreements, Alvotech will repay the aggregate amount of €17.4m that Alvotech had previously received from Stada under the terminated agreements within 20 business days," the biosimilars developer disclosed. Other than any Stada trademarks, all rights connected to the products will revert back to Alvotech.

Stada had first allied with Alvotech back in 2019, with the pair striking a deal covering seven Alvotech biosimilars across major European markets as well as in certain other territories (*see sidebar*).

Alvotech And Stada Make Biosimilars Pact

By David Wallace

07 Nov 2019

Alvotech and Stada have struck a deal that will give Stada exclusive rights to sell seven Alvotech biosimilars "in all key European markets" as well as certain other territories.

Read the full article here

Despite the three terminations, "the other agreements between Alvotech and Stada that pertain to AVT02, a biosimilar to Humira (adalimumab), AVT04, a proposed biosimilar to Stelara (ustekinumab), and AVT06, a biosimilar candidate to Eylea (aflibercept), were not terminated or amended," Alvotech specified.

Stada has already begun marketing the Hukyndra 100mg/ml higher-strength adalimumab biosimilar in Europe – starting a phased roll-out more than a year ago (Also see "*Stada And Alvotech Launch Higher-Strength Adalimumab In Europe*" - Generics Bulletin, 9 Jun, 2022.) – and

has also filed ustekinumab with the European Medicines Agency, with an approval anticipated as soon as the second half of this year. (Also see "*Stada And Alvotech Eye Potential EU Ustekinumab Nod This Year*" - Generics Bulletin, 9 Feb, 2023.)

In the wake of the terminations, a Stada spokesperson confirmed to *Generics Bulletin* that "Stada and strategic partner Alvotech have mutually agreed to amend their biosimilar collaboration, to which both parties remain fully committed."

"Stada will retain commercial rights in the previously disclosed territories to the already approved Hukyndra (adalimumab) biosimilar as well to ustekinumab and aflibercept candidates at the clinical development and/or regulatory assessment stage," the firm outlined. Meanwhile "Alvotech will regain commercial rights to three other biosimilar development programs relating to denosumab, golimumab and vedolizumab."

"For Stada, these amendments preserve commercial rights to two high-value biosimilar candidates, while providing cash through refunded development payments and relieving the group of considerable capital expenditure commitments that can now be redeployed for other projects," Stada explained.

Meanwhile, "Stada's biosimilar commercial and development projects with other partners are not affected by the revised agreement with Alvotech," with the firm insisting that it "remains fully committed to improving patient access through biosimilar competition."

...And Ends BiosanaPharma Deal Amid Pipeline Updates

Also among Alvotech's recent disclosures was an announcement that it had "provided BiosanaPharma a notice of termination for the global licensing agreement between the two companies covering the co-development of AVT23, a proposed biosimilar to Xolair (omalizumab)."

The deal – announced in early 2022 (*see sidebar*) – was the first Alvotech proposed biosimilar that was not developed in-house.

Speaking about the terminated omalizumab development program during Alvotech's first-quarter results call, Anil Okay did not elaborate on the reasons for the termination but said the company was "currently evaluating our alternative options for the program and intend to provide further updates as we finalize the

Alvotech In-Licenses Xolair Rival From BiosanaPharma

By David Wallace

02 Feb 2022

Alvotech has delivered on indications that it would look to collaborate on certain biosimilar opportunities in future, striking a licensing deal with BiosanaPharma that will

strategy."

Meanwhile, commenting on the newly-disclosed Entyvio (vedolizumab) and Keytruda (pembrolizumab) biosimilars in Alvotech's pipeline, Okay said the AVT16 vedolizumab candidate was targeting "a leading immunology product with over $5bn in global sales in 2022" that "has shown significant growth since the product's launch. Current analyst estimates view the growth potential for the brand to exceed $8bn," he suggested.

see the two firms partner to co-develop an omalizumab biosimilar rival to Xolair.

Read the full article here

> ***"[Pembrolizumab] is our first disclosed product in the oncology space, which is an area we intend to expand further into as we continue to build our pipeline."***

And the AVT33 pembrolizumab product was aiming at an even bigger target. "With worldwide sales in 2022 of over $20bn, Keytruda is in the top five products globally in terms of revenue," Okay observed.

He added that "AVT33 is our first disclosed product in the oncology space, which is an area we intend to expand further into as we continue to build our pipeline. The program has completed our clone selection phase and again, we look forward to providing updates on this exciting opportunity going forward."

Meanwhile, Okay also noted that Alvotech had already initiated patient studies for the AVT05 golimumab rival to Simponi and Simponi Aria, brands that brought in more than $2bn in 2022.

"On AVT05, we are currently aware of only one other company that has a clinical stage asset for a biosimilar to Simponi," he stated. "And we are the only company with a clinical stage asset for golimumab that has launched biosimilars in multiple global markets." (Also see "*Alvotech's Simponi Rival Begins Pharmacokinetic Study*" - Generics Bulletin, 16 Jan, 2023.) (Also see "*Alvotech's Simponi Biosimilar Steps Into Phase III RA Study*" - Generics Bulletin, 5 May, 2023.)

China's Bio-Thera Solutions has previously disclosed that it has a golimumab candidate in Phase III trials. (Also see "*Bio-Thera Conducts Simponi Phase III Trial*" - Generics Bulletin, 9 Jun, 2021.)

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Awaiting Further Developments On US Adalimumab

Finally, one other topic that was addressed candidly during Alvotech's recent first-quarter results call was the pending US Food and Drug Administration action on the company's AVT02 adalimumab 100mg/ml candidate.

A succession of complete response letters from the FDA linked to inspections of Alvotech's Reykjavik facility have resulted in delays to approval for the Humira rival, with the latest FDA goal date of 28 June being just days ahead of Alvotech and US partner Teva's planned launch date of 1 July, under a settlement with originator AbbVie (*see sidebar*).

"We remain committed and focused to bringing AVT02, a proposed high-concentration, interchangeable biosimilar to Humira, to patients in the US, after regulatory approval," said Wessman.

Alvotech's Latest FDA Knockback Cuts It Fine For Humira Rival

By David Wallace

14 Apr 2023

Alvotech has received a further complete response letter from the US FDA relating to its AVT02 proposed adalimumab biosimilar rival to Humira. The latest BsUFA goal date disclosed for the product is now just a few days ahead of a potential US launch.

Read the full article here

He insisted that the firm would "continue to work collaboratively with the FDA regarding both biologic license applications for AVT02" – two BLAs were submitted in parallel, with one geared towards also obtaining an interchangeability designation – "and are preparing for all possible scenarios, including resubmission of the first AVT02 BLA and hosting a possible reinspection of our manufacturing facility, which we would anticipate in 2023, if needed."

With the FDA having reviewed the submissions and with the only outstanding requirement being a satisfactory site inspection, Wessman said Alvotech had already submitted requests to the agency to gain further clarity on the status of its deficiencies in the light of responses already submitted by the company, as well as providing monthly updates to the FDA in line with commitments made as part of these responses.

An update due on 1 June "in our view will complete outstanding corrective and preventive actions that we were committed to," Wessman said. And "subsequent to that, the company intends, as a matter of procedure, to resubmit the biosimilar BLA, which would trigger a six-month review period that would be needed in case approval is not granted on June 28, which is the goal date for the interchangeable BLA."

Meanwhile, he pointed out, AVT02 had already been launched "into 17 markets, including Canada and across Europe, without any negative safety signal to date." These adalimumab sales

generated turnover of $15.9m for Alvotech in the first three months of 2023.

Alvotech's Q1 R&D expenses were up 8% at $50.9m, driven by a one-time charge of $18.5m relating to the termination of the Biosana deal and a $10.5m increase in direct program expenses mainly from three biosimilar candidates: AVT03 denosumab, AVT05 golimumab and AVT06 aflibercept, that entered clinical development over the past couple of years. However, these increases were partially offset by a decrease in spending of $13.8m, primarily related to programs for which clinical activities were winding down.

Editor's note: this article was updated on 25 May to add financial details of the Advanz partnership.