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Generics Bulletin Explains: After Humira Biosimilars, Will It Be Groundhog Day For Stelara?

Could Familiar Product Profile And Settlements Framework Mean A Rerun Of Adalimumab?

by David Wallace

With ustekinumab biosimilars set to launch in Europe imminently and in the US early next year, the off-patent industry may be wondering whether it will be in for a rerun of its experiences with competition on Humira – or whether the landscape has changed sufficiently to allow for different pricing and uptake trends. *Generics Bulletin* looks at the expectations of a host of industry leaders.

In the 1993 film *Groundhog Day*, Bill Murray starred as Phil Connors, a man condemned to the repetition of living the same day over and over again. With biosimilar competition to Stelara (ustekinumab) on the horizon, the off-patent industry may be wondering whether to expect a similar fate.

The parallels between Stelara and Humira (adalimumab), which has already faced biosimilar competition around the world, are multiple. The two juggernaut immunology biologic brands share a similar profile, while the lead-up to competition for both has seen a framework of legal settlements agreed with the originator – in the case of Stelara, Johnson & Johnson's Janssen – to allow for market entry around the world.

As is expected to be the case for Stelara, Humira saw staggered biosimilar competition worldwide as adalimumab rivals launched at different times in different regional markets.

In Europe, the simultaneous launch of multiple Humira biosimilars in late 2018 saw fierce

competition lead to immediate heavy price pressure. (Also see "*Four adalimumabs compete in EU*" - Generics Bulletin, 26 Oct, 2018.)

Meanwhile, in the US – where Humira rivals launched from early 2023 onwards – similarly steep discounts were coupled with slow uptake that saw adalimumab biosimilars take almost a year to begin making serious inroads into AbbVie's market share. (Also see "*The Comeback Begins? Positive Signs Seen For Humira Biosimilars In US*" - Generics Bulletin, 22 Apr, 2024.)

A $10bn Target: Stelara Sales Break Barrier Ahead Of Biosimilar Launches

By David Wallace

26 Jan 2024
With competition to Stelara due to kick in midway through 2024, the brand now represents a $10bn+ target for biosimilars, according to the latest figures from J&J.

Read the full article here

And if the onset of biosimilar competition to Humira in the US represented the largest ever loss-of-exclusivity opportunity in the off-patent industry's history – with the market valued at around $17bn – then Stelara is almost as big a target. (Also see "*Humira In 2023: The $17bn Biosimilar Opportunity*" - Generics Bulletin, 5 Jan, 2023.)

Stelara brought in $10.9bn for Johnson & Johnson in 2023, up 11.7% over 2022's $9.7bn (*see sidebar*). In the US, sales grew by 9% to $6.97bn; while internationally, the brand achieved $3.89bn in sales, a 16.7% improvement over 2022.

Humira Biosimilars Have Been 'Paving The Way' For Stelara Competition

In the 1993 film *Groundhog Day*, Bill Murray starred as Phil Connors, a man condemned to the repetition of living the same day over and over again. While initially not recognising his predicament, he soon began to register the repeated events and exchanges that signified that he was reliving his previous experiences.

Similarly, for the off-patent industry, the commonalities between Humira and Stelara competition have been difficult to ignore. Cardinal Health's director of biosimilars, Dracey Poore, summed up the situation succinctly when she told *Generics Bulletin* earlier this year that "we believe that the Humira biosimilar market is paving the way for the Stelara biosimilar entrants." (Also see "*'Parity To The Originator Is Not Enough' – Cardinal Health Talks US Biosimilars*" - Generics Bulletin, 19 Mar, 2024.)

As with Humira, the launch of biosimilars to Stelara is expected first in Europe and then later in the US, albeit with not quite the same wait as the near five-year gap seen with adalimumab.

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In Europe, market formation is expected from the end of July, when a key supplementary protection certificate protecting Stelara expires. Partners Alvotech and Stada have already indicated that they expect to launch their approved Uzpruvo version from late July. (Also see "*Stada And Alvotech Eye Launch Date For Ustekinumab After EU Approval*" - Generics Bulletin, 10 Jan, 2024.)

Other European Medicines Agency-approved ustekinumab biosimilars include Samsung Bioepis and Sandoz's partnered Pyzchiva version and Amgen's Wezenla, while Celltrion's Steqeyma has been granted a positive opinion from the EMA's Committee for Medicinal Products for Human Use that has yet to be converted into a formal marketing authorization by the European Commission. (Also see "*More Stelara Biosimilars Line Up For Launch In US And EU*" - Generics Bulletin, 1 Jul, 2024.)

Meanwhile, in the US three biosimilars have been approved by the US Food and Drug Administration ahead of expected launches in early 2025. These are Amgen's Wezlana (ustekinumab-auub); Alvotech's Selarsdi (ustekinumab-aekn), which will be commercialized by Teva in the US; and the Samsung Bioepis-Sandoz Pyzchiva version.

However, more than just three biosimilars sponsors have already settled with J&J, representing both approved and as-yet-unapproved products alike.

So far, US launch dates under publicly-disclosed settlements include frontrunner Amgen with 1 January 2025; followed by Alvotech and Teva on 21 February; alongside Sandoz and Samsung Bioepis a day later, on 22 February.

Celltrion has settled on terms that allow launch from 7 March 2025; partners Fresenius Kabi and Formycon from 15 April; and Accord from 15 May 2025.

Meanwhile, Biocon Biologics has not disclosed a specific launch date, but said earlier this year that it had settled on terms allowing a launch in February 2025 (*see sidebar*).

Biocon Stelara Settlement Places Firm Among Earlier US Rivals

By David Wallace

01 Mar 2024

Biocon Biologics has secured a launch date for its planned US biosimilar to Stelara that puts it ahead of some of the competition.

Read the full article here

> *"I think ustekinumab will probably behave in a similar way. I would expect the originator to follow relatively similar tactics and again would expect the market to evolve and build, rather than rapidly convert."*

In terms of how the dynamics of the biosimilar ustekinumab market will play out, Sandoz CEO Richard Saynor offered his predictions as the firm delivered its annual results in March. (Also see "*Sandoz Benefits From Betting Big On Biosimilars*" - Generics Bulletin, 14 Mar, 2024.)

Compared to adalimumab, "I think ustekinumab will probably behave in a similar way," Saynor said. "I would expect the originator to follow relatively similar tactics and again would expect the market to evolve and build, rather than rapidly convert," meaning for biosimilars suppliers "a build rather than a bang, over many quarters."

Biocon Biologics' chief commercial officer for advanced markets, Matt Erick, also spoke about his expectations for Stelara competition in an interview with *Generics Bulletin* earlier this year. (Also see "*Biocon Biologics: US Biosimilars Are A Marathon, Not A Sprint*" - Generics Bulletin, 13 Mar, 2024.)

With the firm's settlement "pulling us into that first wave in February 2025," he underlined, "I think that puts us in a really good position as things get started out of the gate," suggesting that "with biosimilars, getting yourself in an incumbent position is always beneficial." And this would be in particular "a key advantage in ustekinumab, when you think about the number of players – the first wave is important."

He further suggested that a second key aspect for suppliers would be their ability to "weather choppy waters" in the event of initial fierce competition, so that "when you get to the other side, when you have calmer waters in the morning of dawn, [you are] able to capture those opportunities as the market starts to settle and play out."

However, for Chrys Kokino – president of Accord US – the first-mover advantage was overstated. While also seeing "multiple parallels" between Humira and Stelara competition, he suggested that stakeholders were "still in a 'wait and see' mode." And "when the Stelara molecule comes out, ustekinumab, there will be another series of 'wait and see' as payers, insurers and wholesalers decide who are they going to partner with and who's going to offer them the best deal."

So "although the different settlement dates have already been announced, there still will be this 'wait and see' approach because everyone's looking to get the best deal," he suggested. "Why would I partner with you in January when I know your competitor's coming out in April? I'm going to wait and see what the best offer is." (Also see "*'The US Is Catching Up' – Accord's Kokino On Biosimilar Market Dynamics*" - Generics Bulletin, 8 Mar, 2024.)

> ***"As the years have gone by, and more healthcare providers have become more comfortable using biosimilars, interchangeability is not as important as it used to be."***

Another factor that not all stakeholders may agree on is the importance of the FDA's interchangeability designation – especially in a context in which the difference between a biosimilar and an interchangeable biosimilar is increasingly downplayed and minimized. (Also see "*Biosimilar Interchangeability Designation Would Be Nixed Under Biden Proposal*" - Generics Bulletin, 12 Mar, 2024.)

This is despite interchangeability – which allows for pharmacy-level substitution, subject to state law – being of particular significance for products like Humira and Stelara that operate in the retail pharmacy channel.

"Ten years ago, our focus was on interchangeability," Accord's Kokino indicated. "The reason for this is because we believed that having an interchangeable designation would lead to accelerated switches from the originator product to the biosimilar." However, "as the years have gone by, and more healthcare providers have become more comfortable using biosimilars, interchangeability is not as important as it used to be."

Alvotech, however, is still a little more convinced of the importance of interchangeability, and hopes to gain a designation for its Teva-partnered Selarsdi version soon after the launch of Amgen's Wezlana, which has already been approved as interchangeable.

"Certainly I think, worst case, we believe we should get interchangeability shortly after our launch," Alvotech chief strategy officer Ming Li told *Generics Bulletin* earlier this year. (Also see "*Alvotech Sees Opportunities Open Up With US Approvals*" - Generics Bulletin, 12 Mar, 2024.)

Meanwhile, Alvotech chief commercial officer Anil Okay highlighted the opportunity for ustekinumab biosimilars to provide an even greater savings potential than adalimumab

biosimilars offered. "I think one thing to point out is that Stelara is probably two times more expensive a treatment than Humira, per year per patient, which makes it an even more attractive biosimilar target for the value chain, as biosimilars bring significant saving to the system," he pointed out.

"Also, another difference is that you don't have an autoinjector platform – Stelara is mostly pre-filled-syringe and vial driven, which makes it also a unique market approach," Okay highlighted. But "overall it's still a retail product," he said, "so it'll be formulary and non-private label type of business…so the dynamics are pretty similar. The payer profiles are very similar."

Li also added that due to the high price of Stelara, ustekinumab biosimilars "could see more dramatic volume growth in ex-US markets." Recalling that "when adalimumab biosimilars were launched in Europe, there was double-digit volume growth for multiple years in a row," he said "we expect something similar in the Stelara market, being that it's potentially underserved in many markets around the world."

Tom Rainey, Teva's senior vice president of US market access, concurred. "This is a really big opportunity, I think, for Teva to reduce healthcare costs," he told *Generics Bulletin*. (Also see "*'At The End Of The Day, It's A Huge, Huge Opportunity' – Teva's Rainey Talks Stelara*" - Generics Bulletin, 15 May, 2024.)

"And if you look just at the [Stelara] 90mg pen," he pointed out, "that's about almost $28,000 or $27,000. Now that's a WAC [wholesale acquisition cost] price, but at the end of the day, it's a huge, huge opportunity to go out and help patients that are taking Stelara and bring it at a reduced cost."

Will The Environment For Biosimilars Improve?

In the 1993 film *Groundhog Day*, Bill Murray starred as Phil Connors, a man condemned to the repetition of living the same day over and over again. Although initially seeming doomed to relive it forever, escaping his purgatory ultimately relied on him using the knowledge gained from his experience to change things for the better.

For developers, the ability to change the entire operating environment for biosimilars may not be completely in their hands – but the ability to learn from past experiences and refine their strategy to better position themselves for success most definitely is.

Speaking to *Generics Bulletin* recently, Celltrion USA's chief commercial officer, Tom Nusbickel, said the firm had already learned lessons from its US launches so far – including adalimumab – that it

'In It For The Long Haul' – Celltrion

would "apply to our products in the PBM space, like ustekinumab."

For example, the gradual move of some suppliers to adopt dual pricing options for their adalimumab biosimilars – offering both a low-WAC option and a high-WAC-high-rebate version to suit the preferences of pharmacy benefit managers – would almost certainly feature upfront in Celltrion's strategy for its ustekinumab biosimilar.

"It does look like with the amount of competition in ustekinumab, the PBMs would like to have both options for their customers," Nusbickel indicated (*see sidebar*). "There certainly seems to be a desire from all three to see that. I think having the optionality is important."

But Nusbickel observed that the PBMs were "also moving in other directions, with their own private labels too," like Cordavis's recent deal for an own-brand adalimumab. So I think that'll be a little bit of a landscape change." (Also see "*Adalimumab Uptake Set For A Boost As CVS Drops Humira From Formularies*" - Generics Bulletin, 9 Jan, 2024.)

> ***"You won't see that slow uptake that you've seen with the adalimumab market because everybody kind of knows what they're doing now."***

Teva's Rainey, meanwhile, was optimistic that all stakeholders were learning lessons from their experiences with Humira and adalimumab biosimilars, meaning that the path would be smoother for Stelara competition.

"The market's evolving as we speak," he suggested. "I think that what's happened is the payers have the right recipe, manufacturers are aligned. You have the clients – when I say the clients, the payers' clients, which are the employer groups – are now becoming more aligned and have a better understanding of what they expect."

Remains Committed To US Biosimilars

By David Wallace

24 Jun 2024

Almost a year after launching Celltrion's Yuflyma rival to Humira in the US, Tom Nusbickel, chief commercial officer of Celltrion USA, reflects on experiences in the market so far and key launches on the horizon, in an exclusive interview with *Generics Bulletin*.

Read the full article here

"And I think now that they have the right recipe for these types of agents," he said. So in future, "you won't see that slow uptake that you've seen with the adalimumab market because everybody kind of knows what they're doing now."

"I think now that as biosimilars start to enter the market, you'll probably see a quicker uptake as you go forward. And that's exciting."

> *"I think the PBM market is going to break up."*

Another major player in the biosimilar ustekinumab market is Formycon, which is partnering with Fresenius on a Stelara rival. And for Formycon CEO Stefan Glombitza, the product held "strong potential" despite potential warning signs from the initial sluggishness of the US biosimilar Humira market.

There were three reasons why the CEO anticipated success. "Number one, I think the PBM market is going to break up," he suggested (*see sidebar*). "Number two, the settlements put us in the position of a lead group in the launch. And number three is that with Fresenius Kabi we really have a strong partner."

Acknowledging the initial "slow adoption rates of adalimumab" in the US, despite multiple biosimilar rivals to Humira being available, Glombitza suggested that "the good thing in this situation is it's really a wake-up call for all the players, all the stakeholders, companies, governments, they all have to learn from that."

'A Global Movement For More Democracy In Medicine' – Formycon Chief Talks Biosimilars Strategy

By David Wallace

15 Apr 2024

Characterizing biosimilars as a global movement towards the democratization of medicine, Formycon CEO Stefan Glombitza speaks to *Generics Bulletin* in detail about the company's recent deals, launches and key pipeline assets, in the first part of an exclusive two-part interview.

Read the full article here

"And I think there will be a learning and there will be more stringent measures to really increase the access and boost biosimilars," Glombitza said. "I'm convinced. I mean that's happening already in the buy-and-bill segment where you have adoption rates of up to 80% since years in the US, two to three years in the market for biosimilars. And the PBM market has to follow and

will follow that way. It's just a matter of time."

"Sustainability comes with education," he summarized, "and the more that all the stakeholders are learning how important the access and the boost for biosimilars is, the better it will be, and the more easy this market will be, and the PBM channel will be accessed. So in the end I think it's just a matter of time."

> ***"I think that the story of the Humira biosimilars, the lack of access to the Humira biosimilars, is on CMS's mind – and I think that is really important."***

Finally, for Julie Reed, executive director of the US Biosimilars Forum, a key part of the puzzle will revolve around Stelara's position on the US price negotiation list under the Inflation Reduction Act. (Also see "*Price Negotiation Purgatory: Upcoming Biosimilars Couldn't Keep Stelara, NovoLog Off The List*" - Pink Sheet, 29 Aug, 2023.)

"The Stelara story not only is about the access to the marketplace, but it's also going to be: will Stelara come off the Medicare negotiation list?" she suggested to *Generics Bulletin* in an interview earlier this year (*see sidebar*).

"If the biosimilar launches, and it should, CMS [Centers for Medicare & Medicaid Services] has laid out that in comments they've made that – and we're looking for the '27 guidance to confirm this – but that it should come off the list if the biosimilars launch at the right time."

Biosimilars Forum Sees Lessons Being Learned From US Humira Experience

By David Wallace

05 Mar 2024

In an interview with *Generics Bulletin*, Julie Reed, executive director of the US Biosimilars Forum, says that the low uptake for Humira rivals in the US has "raised everyone's attention to what is going on and what is wrong with the system."

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But the other piece that CMS has been depending on is what they put in the rule about bona fide marketing; they have not defined it to a point where everyone can say, 'bona fide marketing equals X'."

"And I think that the story of the Humira biosimilars, the lack of access to the Humira

biosimilars, is on CMS's mind – and I think that is really important," Reed said

She suggested that CMS could "make a statement on that bona fide marketing to say, 'hey, look, Humira, it didn't get on the list, but if we thought about it differently, it's not okay that there's no access to the biosimilar to compete'. That's the whole purpose of the special rule and the delay is that the biosimilar has to be able to compete and have market access. It's not okay just to launch."

So "I think CMS and Medicare Part D is part of the issue," she summarized. "They did not look to see if they were providing access to the Humira biosimilars. I think they're learning a lesson, and I think Medicare is going to use its tools that it can, including negotiation, to say we expect robust competition – because the whole delay was based on the fact that through biosimilar competition, Medicare would get savings."

"When the Stelara [biosimilars] launch, we'll know if CMS will have a stronger signal about what they're expecting to see."

In the 1993 film *Groundhog Day*, Bill Murray starred as Phil Connors, a man condemned to the repetition of living the same day over and over again. While Connors eventually manages to take control of his future and escape from a seemingly endless cycle, it remains to be seen whether the same will be true for suppliers of Stelara biosimilars – but stakeholders appear optimistic that a repeat of their Humira experiences is not an inevitability.