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Biohaven looks to seize a new opportunity

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The post-Pfizer pipeline looks disparate, but the group insists there is a method to its fast-follower approach.

After achieving the holy grail of a big pharma buyout, what's next for the biotech left behind? If Biohaven is anything to go by, the answer is: assemble a new pipeline of projects that do not seem to have much in common.

The company's chief executive officer, Vlad Coric, tells *Evaluate Vantage* there is a method to Biohaven's apparently scattergun approach, however. "We want to be able to make an improvement on de-risked mechanisms," he says of the firm's "fast-follower" strategy.

This worked to great effect with Nurtec, the oral CGRP inhibitor that followed injectable products and was the main driver behind Pfizer's $11.6bn swoop for Biohaven last year. Following the deal, the target's remaining assets were spun off into "new Biohaven".

In this respect, Biohaven looks a lot like Nimbus, which is also continuing following a big-league buyout. However, there are some major differences between the groups: Nimbus is private while Biohaven is public, and Nimbus has relied on internal development while much of Biohaven's pipeline has come from deals.

Better than Xenon?

A major focus for the new incarnation of Biohaven is BHV-7000, gained via the 2022 acquisition of Channel Biosciences and being developed for epilepsy; it also has potential in mood disorders. The Kv7 potassium channel activator is designed to be a step up from others in this class, specifically in terms of adverse effects, which Dr Coric puts down to the older drugs' effects on the neurotransmitter Gaba.

A first-generation Kv7 activator, GSK's Potiga (ezogabine), was approved in 2011 but later withdrawn following concerns about vision loss and bluish skin discolouration. Xenon's next-gen compound, XEN1101, was not linked with these problems in its phase 2 trial but Dr Coric believes there is still room for improvement in terms of Gaba-ergic side effects like dizziness, somnolence and fatigue.

He says that, with BHV-7000, Biohaven has "dialled out the Gaba effects". He points to phase 1 safety data, unveiled at the JP Morgan healthcare conference in January, saying: "We did not have adverse events in those categories."

Still, Xenon claims XEN1101 has no activity on Gaba-A receptors, SVB analysts noted, raising the possibility that these side effects might be down to another mechanism.

Ultimately, with BHV-7000 Biohaven wants to see similar efficacy to XEN1101 but with better tolerability. Biohaven expects more phase 1 data this year, and plans to start a pivotal trial in focal onset seizures in the second half. Xenon's XEN1101 is already in the X-tole-2 phase 3 trial for this use. Both companies also have plans in depression.

Another shot at myostatin

Meanwhile, with its myostatin inhibitor taldefgrobep alfa, Biohaven hopes to follow the path forged by another rival, Scholar Rock, which reported promising data from the phase 2 Topaz trial of apitegromab in spinal muscular atrophy in 2021. Myostatin inhibition has not always worked out – in fact, Biohaven licensed taldefgrobep alfa from Bristol Myers Squibb following its failure in the Spitfire study in Duchenne muscular dystrophy, conducted by Bristol's former partner Roche.

Dr Coric believes that, in hindsight, DMD might not have been the best disease to target with this approach, and points to intriguing results from Spitfire, which found an increase in muscle mass but no improvement in function. "We know this compound does cause muscle growth. Unfortunately, what we found out in DMD is that if you don't treat the underlying muscle disorder, growing more muscles is likely not to benefit you."

It is notable that both apitegromab and taldefgrobep alfa are being tested in their pivotal trials on top of existing SMA therapies, Spinraza, Zolgensma and Evrysdi. "We believe you have to treat the underlying cause of the disease. And then you would benefit from bolstering the muscle mass to increase function," Dr Coric says.

Others have not given up on hitting myostatin, including Roche with RG6237, also in late-stage development in SMA. While apitegromab and RG6237 both target latent myostatin, taldefgrobep alfa inhibits both active myostatin and the downstream ActIIRB pathway. SVB suggests that this could lead to greater efficacy, but raises the concern that reduced selectivity could mean more adverse events.

Troriluzole hangs on

While taldefgrobep alfa looks like a high-risk bet, there is even more doubt about Biohaven's lead project, troriluzole. Despite a phase 3 failure in spinocerebellar ataxia last year, the group still hopes there is a path forward here in a subgroup of patients with the SCA3 genotype, who account for 40-50% of the population. Biohaven plans to get feedback from the FDA this half.

Pivotal results are also coming in obsessive-compulsive disorder, but again this looks like a long shot given previous failures in this disease. Dr Coric reckons that the phase 2 trial was underpowered, and that bigger pivotal studies will lead to a result.

Troriluzole seems unlikely to repeat the success of Nurtec, but the chief exec insists he doesn't have one eye on another buyout. "You have to run your business like you're going to own it forever. That's our strategy."

Biohaven's clinical/near clinical pipeline		
Project	**Description**	**Trial details/note**
Troriluzole	Glutamate modulator	Failed ph3 in spinocerebellar ataxia but company to discuss with regulators; ph3 trials in OCD (NCT04641143 & NCT04693351) to read out 2023/2024; ph2/3 GBM Agile* in glioblastoma
Taldefgrobep alfa (BHV-2000, prev RG6206)	Myostatin inhibitor	Ph3 Resilient in SMA as add-on to SOC; data likely 2024
BHV-7000	Kv7 potassium channel activator	Ph1 in focal epilepsy, final data due H1 2023; ph2/3 to start H2 2023
BHV-1100	Anti-CD38 x Ig bispecific (recruits NK cells)	Ph1/2 completes Jun 2023
BHV-1300	IgG degrader	IND anticipated 2023 (indication undisclosed)
BHV-2100	TRPM3 antagonist	IND anticipated 2023 (chronic pain)
BHV-7010	Kv7 potassium channel activator	IND anticipated 2023 (epilepsy & mood disorders)

**Investigator-sponsored trial. Source: Evaluate Pharma, clinicaltrials.gov & company presentation Jan 2023.*