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# Boehringer pushes pipeline progress

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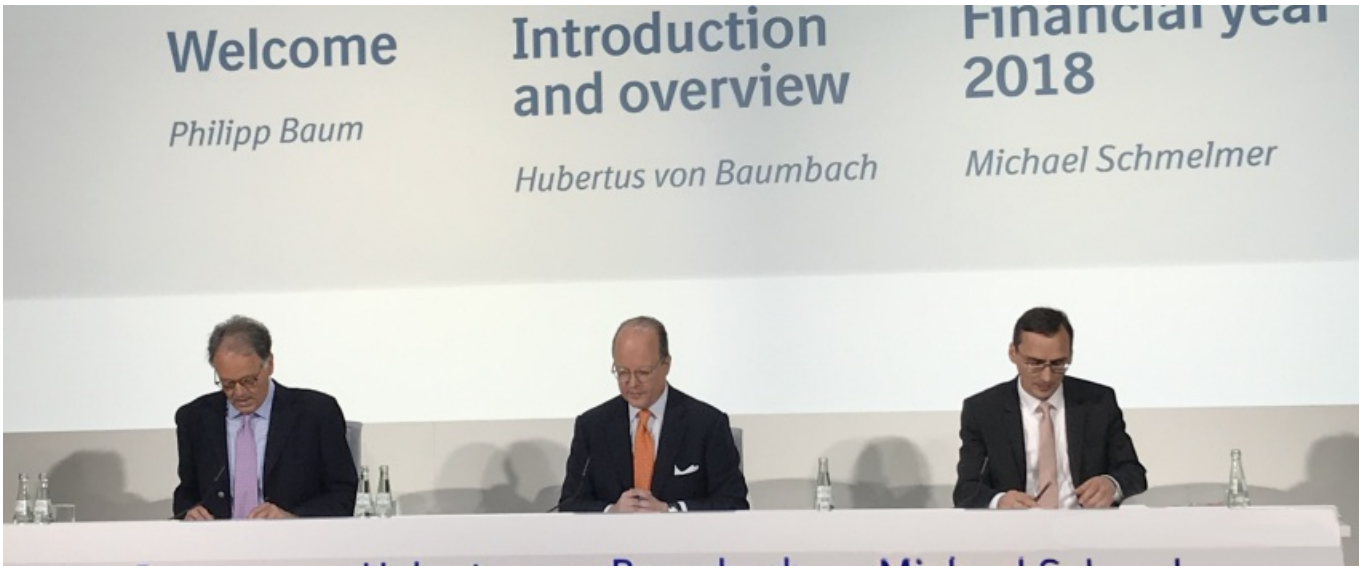


**The notoriously secretive German pharma company Boehringer Ingelheim has made much of a new drive towards transparency, but there are still things it would rather keep to itself.**

This time last year, Boehringer Ingelheim gave a rare insight into its pipeline. It did not put as much on show at its annual press conference this week, but was keen to highlight progress with its top pipeline prospects in areas such as psoriasis, Nash and oncology.

However, Boehringer still seemed reluctant to reveal all about one of its brightest hopes, the IL-36 inhibitor spesolimab. The group made a big splash in March with positive data in the project's lead indication, generalised pustular psoriasis – but has been cagey about results in a bigger use, palmoplantar pustulosis (PPP).

**Spesolimab subgroup analysis**

A 59-patient phase II trial in PPP was completed in July 2018, according to clinicaltrials.gov, but Boehringer has not released any data. Now it seems that disappointing results might be behind the radio silence.

Michel Pairet, head of the group's innovation unit, yesterday told *Vantage* that Boehringer had seen some preliminary results in PPP, and admitted that spesolimab, previously known as BI 655130, did not work so well in patients with less severe disease and fewer pustules – though he questioned whether these patients had true PPP.

Boehringer now plans to focus on more severe PPP patients, who Mr Pairet said responded "particularly well" to spesolimab. He added that the full PPP trial results would be released, but would not say exactly when.

The link between IL36 mutations and disease is stronger in generalised pustular psoriasis (GPP) than in PPP, so perhaps it would not be surprising if spesolimab worked better in the former. But GPP is very rare, affecting only around 20,000-30,000 patients, and Boehringer would prefer a bigger market for the project, which it hopes will mark its solo entry into the autoimmune space.

Studies of spesolimab are also under way or planned in even broader indications including atopic dermatitis, inflammatory bowel disease and ulcerative colitis. If Boehringer is already dredging the data to find a positive subgroup in PPP, this might bode ill for these other uses, too.

**Nash combos**

Another big focus for Boehringer is Nash, and here its lead candidate is BI 1467335, an AOC3 inhibitor acquired from Pharmaxis. This project is designed to reduce the inflammation thought to contribute to the liver disease.

Boehringer has completed enrolment into a phase II trial, and expects to report data in September or October, Mr Pairet said. He added that the company hoped to show a result on Nash resolution, but that a benefit in fibrosis would be a bonus.

Other groups are looking at different mechanisms in Nash, with some disagreement over which strategy – targeting inflammation, fat accumulation or fibrosis – might ultimately prove most successful

Like many of its peers, Boehringer believes that a combination approach will be needed, and is keen to have all the components in house. As well as BI 1467335, Boehringer is developing a soluble guanylate cyclase inhibitor to target fibrosis, and a GLP-1/glucagon co-agonist to modulate lipid metabolism, according to Mr Pairet.

The former is not listed in Boehringer's pipeline, while the latter is down as an unnamed phase I project.

Mr Pairet added that Boehringer and Lilly's SGLT2 inhibitor Jardiance, which is marketed in type 2 diabetes, should not be ruled out as part of a Nash combo. The potential of diabetes drugs in Nash was underlined last week in a deal between Gilead and Novo Nordisk (*EASL 2019 – Novo buys into Gilead's Nash combo plan, April 12, 2019*).

**Immuno-oncology ambitions**

The other big area in which Boehringer wants to become a player is immuno-oncology, although it has previously admitted that it had missed the checkpoint inhibitor monotherapy wave. The group is therefore focusing on combinations with its in-house anti-PD-1 MAb BI 754091.

In common with other players Boehringer wants to turn "cold" tumours "hot", but Mr Pairet says it is "one of the very few companies bringing together the different pieces of the puzzle", citing cancer vaccines and bispecific antibodies as important components. Boehringer's purchase of the oncolytic virus group Viratherapeutics last September illustrates its determination to make a mark here.

Beyond I-O, Boehringer has ambitions to hit "undruggable" cancer targets such as KRAS, WNT and mutated p53, and has preclinical projects here. In this arena the German group thinks its recent acquisition of ICD Therapeutics could help by allowing it to take aim at intracellular targets that would otherwise be inaccessible using conventional antibodies or small molecules.

Still, even in the best-case scenario it will be a long while before Boehringer can call itself an oncology contender. In the meantime, it is relying on later-stage projects like spesolimab, which still has plenty of question marks around it.