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# Interview – Boehringer's new look aims to boost innovation

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Boehringer Ingelheim's present might be all about the diabetes drug Jardiance, but the company is also planning for the future. The German group spent 20.3% of its net 2015 sales on R&D – granted, not as much as the biotech companies Regeneron and Celgene, but a higher proportion than many of its big pharma peers (see table below).

The result of its historic R&D investment is a "very promising pipeline", says Michel Pareit, who will be heading up Boehringer's new innovation unit from July. The pipeline is also benefiting from collaborations, an increasing focus for the company. Boehringer has earmarked €1.5bn of its R&D budget for partnerships.

The new innovation division will be responsible for development up to proof of clinical principle, around phase Ib or phase IIa; any asset that makes it this far will then be developed by the more market-oriented prescriptions medicines business.

| Top 10 big pharma and biotech R&D spenders | |
|---|---|
| **Company** | **% sales spent on R&D in 2015** |
| Regeneron | 39.5 |
| Celgene | 24.8 |
| Lilly | 24.0 |
| AstraZeneca | 22.7 |
| Boehringer Ingelheim | 20.3 |
| Roche | 19.4 |
| Biogen | 18.7 |
| Amgen | 18.1 |
| Novartis | 17.4 |
| Merck & Co | 16.7 |

While the innovation unit aims to build on Boehringer's current areas of expertise, the company also wants to be involved in emerging science. "We don't want to miss the next wave of innovation, which [otherwise] might simply take place elsewhere," Mr Pareit tells *EP Vantage*.

The company has a corporate venture fund and a division called research beyond borders, both with the goal of making "smart bets in emerging science, with academic institutes, with biotech". Areas of interest include regenerative medicine, the microbiome, gene therapy and hearing loss.

"But of course we're agnostic, and if something great comes and is completely outside [this] we'll explore it," he says.

**Partnerships**

One way that Boehringer plans to access innovation is through the aforementioned focus on partnerships. "Our current [marketed] product portfolio is 100% based on in-house projects," says Mr Pareit. "But in our current development pipeline 50% of our projects have some level of external innovation."

He highlights the group's third-generation EGFR tyrosine kinase inhibitor licensed from the South Korean

company Hanmi. BI 1482694 is in a phase II trial as a second-line treatment for patients with non-small cell lung cancer with T790M mutations, where it has FDA breakthrough therapy designation. Boehringer hopes for accelerated approval in 2017.

However, here Boehringer is some way behind AstraZeneca, which has had its EGFR inhibitor, Tagrisso, on the market since last year for T790m-mutated NSCLC. Clovis is also looking at the same mechanism and indication with rociletinib, but was recently knocked back by an FDA advisory panel (*Adcom could kill off Clovis's rociletinib, April 13, 2016*).

| Selected early-stage Boehringer pipeline highlights | | | | |
|---|---|---|---|---|
| **Project** | **Status** | **Origin** | **Therapy area** | **Trial details** |
| BI 1482694/ HM61713 | Phase II | In-licensed | Oncology | Eluxa 1, NCT02485652 |
| BI 409306 | Phase II | In-house | Neurology | NCT02337907; NCT02281773 |
| CV9202 | Phase I | In-licensed | Oncology | NCT01915524 |
| PXS4728A | Phase I | In-licensed | Gastrointestinal | N/A |

Boehringer has another interesting collaboration in NSCLC, covering CureVac's mRNA-based cancer vaccine CV9202, which is in a phase I trial in second-line disease.

The company aims to combine CV9202 with its EGFR/HER2 dual kinase inhibitor Gilotrif, which is approved in NSCLC patients with a primary EFGR mutation and also recently got the go-ahead in second-line advanced squamous cell carcinoma of the lung.

But the vaccine could also be combined with immune checkpoint inhibitors, Mr Pareit believes. "We realise we're late in the field of immune checkpoint inhibitors. But we're convinced we can develop a unique positioning via the combination of immune checkpoint [inhibition] with cancer vaccines."

Boehringer has its own checkpoint inhibitors in early development, he says, along with "several collaborations with biotech and academic institutes on next-generation immune checkpoint inhibitors".

But it is not inconceivable that the company could test CV9202 with existing checkpoint inhibitors such as Bristol-Myers Squibb's Opdivo and Merck's Keytruda, he adds. Results from phase II combination studies should report in 2018.

**Next up NASH and Alzheimer's**

Mr Pareit also emphasises PXS4728A, an asset acquired from Pharmaxis last year in another increasingly crowded field: non-alcoholic steatohepatitis (NASH). He believes that Boehringer can capitalise on its presence in other cardiometabolic diseases, such as diabetes, to help it sell the NASH candidate should it get to the market.

But the group is up against stiff competition, not least from the liver disease giant Gilead, which has made its intention in NASH clear with a rash of deals (*Gilead doesn't buy Intercept, April 5, 2016*).

Not all of Boehringer's promising candidates come from collaborations, however. At its recent annual press conference the company talked up the PDE9 inhibitor BI 409306, in development for the treatment of cognitive impairment in Alzheimer's disease and schizophrenia.

The group is taking a different tack to others looking at Alzheimer's, many of which are focused on the amyloid-beta hypothesis. "There are several attractive mechanisms, but almost everybody is working on these mechanisms," says Mr Pareit. "We want to invest in fields where we think we can have a unique position."

Boehringer has decided, within CNS disease, "to have a stronger focus on psychiatric diseases than on neurodegenerative diseases", he adds. BI 409306 is the most advanced PDE9 inhibitor in development, according to *EvaluatePharma*, with Eisai's E2027 next, in phase I.

The company has devoted €11bn to R&D in the next five years; €5bn of this is going to preclinical research. Boehringer will hope the funds as well as its increased focus on early-stage assets will help it outshine its rivals in the years to come.

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