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# Boehringer Strengthens Partner Ecosystem To Drive Early Ophthalmology Innovation

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By David Wild

Boehringer Ingelheim's collaboration with Re-Vana Therapeutics is the most recent step in the German pharma's paradigm shift toward earlier intervention in retinal diseases.

When Boehringer Ingelheim announced its strategic collaboration with Re-Vana Therapeutics in July, the deal represented more than just another ophthalmology partnership.

With a potential value exceeding \$1bn across three initial programs, the collaboration helps Boehringer fulfill its retinal disease strategy: to move from frequent eye injections starting when symptoms have already appeared to a proactive approach rooted in long-acting interventions initiated early in the disease process.



Patrick Bussfeld

## EARLIER AND LESS INVASIVE

Patrick Bussfeld, head of experimental medicine eye health at Boehringer Ingelheim, articulated the transformative approach. "Our treatment approach is to go earlier, to actually protect more retina," he told *In Vivo*.

This shift represents a departure from how anti-vascular endothelial growth factor (VEGF) therapies are currently administered: patients are typically treated only after substantial retinal thickening has already occurred and "a lot of visual tissue has been lost by that point," Bussfeld said.

A shift to earlier intervention would require a complete ecosystem transformation, Bussfeld said. To that end, Boehringer is developing AI solutions for earlier disease detection and working with academic collaborators, patient organizations and regulatory authorities to establish new treatment paradigms. For diabetic patients, for example, this means embedding earlier retinal screening into routine care to reduce the likelihood of vision loss.

In addition to earlier detection, central to the new approach is reducing treatment burden. This is because treating earlier often means patients are not yet fully aware of their risk, have not been affected by the illness, and are thus less motivated to accept invasive procedures. That calls for "oral formulations or intravitreal treatments that provide a longer cadence of treatment," Bussfeld said. This is where Re-Vana's platform became very attractive and brought the two companies to the partnering table.



## RE-VANA'S DIFFERENTIATED PLATFORM

Re-Vana CEO Michael O'Rourke, who has launched two of the first sustained-release intraocular drug delivery products, said his company's technology is based on photo cross-linked biodegradable hydrogel implants. (I.e. light-activated gel matrices that dissolve safely in the eye.) These can deliver a variety of payloads – from biologics to small and large molecules as well as peptides – up to 12 months, the company has found in preclinical *in vivo* models.

Re-Vana overcame three barriers that have historically limited biologic drug delivery in the eye: maintaining protein stability, achieving high drug loading (20-50% by weight) and ensuring excellent tolerability to prevent inflammation-related failures.

"One thing that differentiates us is that we use light, not heat, to prepare the implant, so we do not destroy the protein," O'Rourke explained.

The company's platform comprises three complementary technologies: EyeLief®/EyeLief SD™ (pre-formed implants prepared with ultraviolet light cross-linking) and OcuLief® (liquid drug formulations that, after injection, form implants *in situ* using visible light activation). The technologies can deliver 10-15 milligrams of drug from just 20 microliters of liquid.



Michael O'Rourke

## STRATEGIC RATIONALE

The partnership combines Re-Vana's customizable delivery platform with Boehringer's ophthalmology pipeline:

- a Phase II oral phospholipid modulator for geographic atrophy (BI 1584862), an antibody fragment for geographic atrophy (BI 771716);
- an anti-Sema3A antibody for diabetic retinopathy (BI 764524) that has completed Phase I study; and
- an oral treatment for diabetic macular edema (BI 1815368) currently in Phase II trials.

Re-Vana's ability to tailor its technology to specific targets product profiles particularly appealed to Boehringer.

"Since we have a broad biochemical approach, it was important that the hydrogel formulation provides the opportunity to jointly develop the assets, regardless of chemical structure," Bussfeld noted.

O'Rourke added: "If we know what the target product profile is – how long it's going to deliver, what's the size of the drug what's the solubility – we can customize our technology to the actual product profile."

For Re-Vana, the collaboration is part of a hybrid strategy of pursuing both proprietary assets and partnerships. While it is developing internal programs like a six-month sustained-release version of aflibercept for wet age-related macular degeneration/diabetic macular edema, and a bispecific VEGF product, the company is simultaneously leveraging its platform for collaborations.

"We don't want to be just a drug delivery company," O'Rourke emphasized. "We want to be our own ocular therapeutics company."

## OPERATIONAL STRUCTURE AND EXECUTION

Re-Vana will be responsible for feasibility and early development while Boehringer assumes clinical development, regulatory approval and global commercialization responsibilities. Both companies are maintaining dedicated, firewalled teams for collaboration projects.

"In a partnership between two companies it is always very important that one side knows their deliverable and the other side knows their deliverable," Bussfeld said. Rather than having an overburdensome oversight structure for the partnership, governance relies on "outstanding personal and professional relationships" built during extensive due diligence, he added.

## MARKET IMPACT AND VALUE PROPOSITION

As Bussfeld sees it, the collaboration addresses a massive treatment burden. He estimated that approximately 26-27 million intravitreal injections are performed annually globally, and the average patient receives up to nine injections annually.

The goal of extending treatment to 6-12 months could dramatically reduce the injection burden, with positive benefits for a range of stakeholders. For payers,

the economic implications would extend beyond drug costs. For example, in Germany, transportation costs to injection appointments represent more than a quarter of total treatment expenses covered by government payers related to retinal disease treatment. "These impose a huge cost load on the healthcare system," said Bussfeld.

Reducing injection frequency could also expand treatment access by alleviating capacity constraints. "Injection clinics are packed with people waiting in line," he said. "By enlarging the injection interval, you can actually allow more patients to get treated."

## TRANSFORMING TREATMENT PARADIGMS

Boehringer hopes to launch the above ophthalmology assets by roughly 2030 and is initiating efforts to establish community backing for earlier intervention approaches, potentially making anti-VEGF therapy a second-line option reserved for treatment failures.

Boehringer has entered other collaborations to realize its vision of earlier ophthalmology intervention. It partnered with German-based ZEISS Medical Technology to develop artificial intelligence-powered early disease detection and struck a deal with Swiss/American company RetinAI that specializes in clinical and imaging data management software, to use AI and identify novel biomarkers in geographic atrophy research, potentially identifying the disease earlier.

The company also recently announced a \$327m collaboration with Palatin Technologies to develop melanocortin receptor agonists for diabetic retinopathy, demonstrating its multi-pathway approach to retinal disease treatment.

## RE-VANA INVESTMENT AND GROWTH TRAJECTORY

For Re-Vana, which has raised approximately \$18m across seed, pre-series A, and Series A rounds, the Boehringer collaboration provides crucial validation as it pursues a \$40m Series B round to advance its proprietary aflibercept program.

The company's unique positioning – with scientific operations in Belfast and business leadership in the US – allows access to both European and American markets, while tapping into Northern Ireland's emerging life sciences ecosystem, supported by Queen's University's internal venture capital arm. The company itself is a Queen's University spinout.

While the deal is fresh and specific targets remain undisclosed, pending feasibility assessments, both companies are confident in near-term progress. "We're pretty sure we can move with a certain speed toward the end goal, and we'll see outcomes in a short to midterm phase in the upcoming years," Bussfeld said.

If the strategic revamp proves viable, Boehringer could fulfill a deep unmet need and become a major player in ophthalmology, while Re-Vana would set itself up for additional big pharma deals.