

Programming Proteins for Precision: Skape Bio's Quest to Unlock GPCR Biology

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CEO Dr. Christoffer Norn discusses how computational protein design and native-cell screening are enabling precision biologics for one of medicine's most important yet challenging target classes.



At BIO International Convention 2026 in San Diego, **BioSpectrum Asia spoke with Dr. Christoffer Norn, Co-founder and CEO of Skape Bio, about the company's breakthrough work in designing functional miniproteins against multiple GPCR targets.** Combining artificial intelligence-driven protein design with high-throughput screening in native human cell environments, Skape Bio is pioneering a new class of biologics that could overcome longstanding limitations of small molecules and antibodies. In this interview, Norn shares how these advances are reshaping GPCR drug discovery, the emerging role of designed miniproteins in therapeutics, and the strategic milestones the industry should watch in the years ahead.

Skape Bio recently demonstrated the successful design of functional miniproteins against multiple GPCR targets. What scientific and technological breakthroughs made this achievement possible, and what does it signal for the future of GPCR drug discovery?

Two things made this possible. First, advances in computational protein design now allow us to computationally design proteins for a specific biological function rather than simply screening large libraries and hoping to find something that works. In our case, we can design miniproteins intended to stabilize GPCRs in active or inactive states, allowing us to create agonists and antagonists with a level of precision that has historically been difficult to achieve.

Second, we developed a high-throughput screening platform that allows us to test tens of thousands of designs directly against full-length receptors in living human cells while keeping those receptors in their native membrane environment. That's important because GPCRs are highly dynamic proteins, and many traditional screening approaches alter the receptor in ways that can make it difficult to identify truly functional molecules.

Together, those advances allowed us to generate functional agonists and antagonists across 11 GPCR targets and validate the designs structurally using cryo-EM.

Looking ahead, this signals a shift toward the rationale design of biologics-based therapies for GPCRs, a target class historically dominated by small molecules but underrepresented by biologics. In addition, it may also allow the identification of ligands to intractable or orphan GPCRs which could unlock a large number of new potential drug targets.

Despite being among the most clinically validated target classes, many GPCRs have remained difficult to drug with precision. What are the key limitations of conventional approaches, and how does Skape's platform address these challenges?

Small molecules bind GPCRs but often also bind related family members, causing off-target effects. Antibodies on the other hand, are generally too large to access the orthosteric binding pockets GPCRs use for signaling. As a result, generating agonist antibodies from random screens has proven nearly impossible, and among the few approved GPCR-targeting antibodies, none act as agonists.

The deeper problem is that conventional screening methods weren't built for GPCRs. GPCRs are highly dynamic, membrane-dependent proteins whose conformational equilibria are strongly influenced by their lipid environment. While membrane mimetics such as nanodiscs and liposomes aim to preserve native-like behavior, different systems can still shift receptor conformations compared to the native cellular membrane, and detergent solubilization in particular can significantly perturb GPCR function.. Skape's OPS-RD platform keeps the receptor in its native membrane environment, inside a human cell. Binders discovered through the screen must be efficiently translated, soluble, and specifically bind the target in its natural context. That is what makes the generation of binders that are more likely to translate into functional activity tractable for this target class.

AI driven drug discovery continues to attract significant attention across the biopharma sector. From your perspective, where does artificial intelligence create the greatest value in therapeutic discovery, and where does experimental biology remain irreplaceable?

I think the greatest value AI creates is that it allows us to move from discovering molecules to designing them. Traditionally, drug discovery has been about searching through existing chemical or biological libraries to find something that has the properties you want. What excites me about protein design is the idea that we can start with a biological problem and build a solution from scratch.

At Skape, we use AI to design miniproteins that have never existed in nature and are engineered for a specific purpose. For GPCRs, that might mean designing a miniprotein that stabilizes a receptor in an active state to act as an agonist, or an inactive state to act as an antagonist. We can also begin to design properties such as stability, selectivity, and manufacturability into the molecule from the outset rather than trying to optimize in a more traditional iterative way.

That said, experimental biology remains irreplaceable. Computational models can guide better designs and help prioritize molecules but ultimately, biology determines whether they work. This is especially true for GPCRs, where function matters as much as binding, since molecules can bind a receptor without producing the desired biological effect. I see the future as a combination of both. AI allows us to create and evaluate entirely new classes of proteins with a speed and precision that wasn't possible a few years ago, while experimental biology provides the ground truth that tells us which designs actually work in a living system. The real breakthroughs happen when those two capabilities are tightly integrated.

Your platform combines computational protein design with high throughput screening in native membrane environments. How important is this integration in improving candidate quality, development timelines, and overall success rates?

It is the core of what makes the platform work. The design side generates miniproteins targeting specific receptor conformations, with developability properties built in. But for Class A GPCRs especially, the orthosteric binding sites are deeply recessed and the active and inactive states differ by only a few angstroms. You need to screen at scale to find functional hits against those targets.

OPS-RD can test up to 100,000 designs per campaign. Each cell expresses one design alongside the target receptor; binding causes the receptor to be diverted from its normal trafficking pattern, generating a detectable signal; in situ sequencing reads a DNA barcode inside each cell, linking each signal back to its design across millions of cells. Validated hits then move into in-house pharmacology: functional classification, potency, selectivity, and DMPK. The integration is what allows Skape to move from a computational design to a pharmacologically characterized hit efficiently.

As pharmaceutical companies increasingly seek novel modalities beyond traditional small molecules and antibodies, where do you see designed miniproteins fitting within the broader therapeutic landscape over the next five years?

Miniproteins are a distinct therapeutic modality that sit between small molecules and antibodies. They are typically 40-70 amino acids long, completely de novo designed, and do not rely on a naturally occurring protein scaffold. Because of their small size, they can access binding pockets that are often out of reach for antibodies. In our GPCR programs, some designs penetrate deep into receptor binding pockets below the membrane surface while maintaining high levels of selectivity.

One of the most exciting aspects of the modality is that we can design these proteins from scratch for a specific biological function. Rather than starting with a naturally occurring molecule and optimizing it, we can design a miniprotein to stabilize a receptor in a desired state and then engineer properties such as stability, half-life, and manufacturability around that function.

We have already shown that those properties can be tuned. An unmodified miniprotein is cleared rapidly from circulation, while an Fc-fused version extends exposure by more than 200-fold. That flexibility creates opportunities across a range of therapeutic settings, from localized treatments to chronic diseases where longer duration is important.

Over the next five years, we expect miniproteins to move from early validation into the clinic and begin to establish themselves as a complementary modality alongside antibodies and peptides—particularly in areas where target accessibility and functional precision are limiting for existing approaches.

The modality is still early relative to antibodies or peptide therapeutics, but we believe miniproteins have the potential to become an important new category of medicines. Our Nature paper provides one of the first demonstrations that de novo designed miniproteins can function as GPCR agonists and antagonists, opening the door to targets and mechanisms that have historically been difficult to address with existing approaches.

Looking ahead, what are Skape Bio's strategic priorities for partnerships, platform expansion, and pipeline development, and what key milestones should the industry watch for following BIO 2026?

The Nature paper validates the platform. What comes next is building a pipeline that is commercially attractive and demonstrates differentiation for miniproteins over existing modalities. Rather than focusing on a single indication, we have carefully selected GPCR targets that play a significant role across multiple disease areas with a balance of agonist and antagonist mechanisms. The goal is to demonstrate that miniproteins can consistently deliver precise control of receptor function across different biological contexts, not just in one program.

From a platform perspective, our priority is to continue scaling the generation of high-quality GPCR binders and systematically translating those into differentiated drug candidates. The throughput of the platform allows us to explore targets that have historically been difficult to drug, and to do so across multiple programs in parallel.

Partnerships are a core part of our strategy. Given the breadth of the GPCR landscape, we can pursue more targets than we intend to advance internally, and collaborating with pharma partners is a key way to unlock that capacity and extend the reach of the platform.

Looking ahead from BIO 2026, the key milestones for the industry to watch will be the translation of differentiated miniproteins into drug candidates across multiple programs, and the establishment of initial strategic partnerships that demonstrate the scalability of the platform.