Andrea Chicca – Co-Founder and CEO, Synendos Therapeutics

This is a moment that calls for thoughtful boldness.

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Amid a crowded landscape of incremental innovation, Synendos Therapeutics stands out for its bold approach to neuropsychiatric drug development. Co-Founder and CEO Andrea Chicca shares how the company emerged from a translational research programme in Switzerland to pioneer a first-in-class therapeutic strategy targeting the endocannabinoid system, a master regulator of brain function often overlooked in mainstream approaches. With its lead candidate SYT-510 now completing Phase I trials, Synendos is advancing a data-driven clinical model that transcends diagnostic silos in favour of symptom-focused precision which cuts across neurology and psychiatry indications.

What led you to make the leap from academia to entrepreneurship and establish Synendos Therapeutics?

The path that led to the founding of Synendos was far from linear, shaped by experiences across academic research, industry, and translational science. I initially studied pharmaceutical chemistry at the University of Pisa, followed by a PhD in pharmacology conducted between Pisa and ETH Zurich. Early in my journey, I spent time at Procter & Gamble in Germany, working in the R&D division on a consumer-facing product: a moisturising lotion for Tempo Plus handkerchiefs. While this project was far removed from drug development, it offered an early glimpse into applied

innovation and the satisfaction of solving real-world problems, something that stayed with me.

Still, I returned to academia, completed my doctoral studies, and pursued postdoctoral research in Florence and Switzerland. But over time, I grew increasingly interested in seeing how discoveries move beyond the bench. That curiosity brought me to Chiesi Farmaceutici in 2008, where I joined the early development group within corporate marketing. It was a dramatic shift: on a Friday, I was still in the lab pipetting, and by the following Monday, I was immersed in discussions around product strategy and brand positioning, an entirely new vocabulary and mindset. Fortunately, I remained closely connected to the scientific side, contributing to the transition of molecules from non-clinical to early clinical development and participating in new product evaluations. This blend of science and strategy proved formative.

A few years later, I was invited by my former supervisor to return to academia and join an NCCR (National Centres of Competence in Research) programme in translational medicine. These Swiss government-funded initiatives are ambitious and long-term, designed to bridge basic research and applied development. It was within this framework that we identified a promising new class of neuromodulators with potential therapeutic applications in multiple brain and inflammatory disorders. Over time, the case for taking this work beyond academia became stronger.

Entrepreneurship was not something I had originally envisioned, but as I engaged with the idea, it steadily began to resonate with me. I took courses to build my understanding and joined the BaseLaunch accelerator in Basel, where I gained valuable exposure to the biotech ecosystem. By 2019, I had co-founded Synendos Therapeutics together with Professor Jürg Gertsch and Dr Simon Russell, a business development expert I met through the programme. From a starting point of one, the company has grown into a ten-person team and has successfully brought its lead candidate into Phase I clinical trials, which began in 2024 and are now nearing completion.

What is the overarching mission of Synendos Therapeutics, and how is the company positioning itself to address the broader challenges in neuropsychiatric care?

At Synendos, our core mission is to restore brain function in patients affected by neuropsychiatric disorders, a category of diseases that continues to represent one of the most pressing, yet underserved, global health challenges. These conditions affect over one billion people worldwide, accounting for roughly 15 percent of the global population, and are associated with significant reductions in life expectancy, elevated disability burden, and millions of premature deaths annually. It is a crisis that extends well beyond medicine into the fabric of society itself.

Although several treatment options exist, they often fall short in addressing the full complexity of these disorders. Many compounds provide partial symptomatic relief for a subset of patients, but fail to offer meaningful outcomes for broader populations. Moreover, mental health conditions are typically chronic in nature, requiring long-term treatment; yet many drugs struggle to combine efficacy with tolerability. A significant number of patients discontinue therapy due to side effects, while others find available medications ineffective for their specific condition, leaving a vast unmet need.

Our approach at Synendos begins with a different question: rather than targeting individual neuronal circuits or isolated brain regions, how can we restore the brain's natural balance? We focus on the endocannabinoid system (ECS), a key neuromodulatory network that orchestrates communication between brain regions and neurotransmitter systems. Much like a conductor ensuring an orchestra plays in harmony, the ECS does not generate signals itself but synchronises the various players that together produce coherent brain function.

In neuropsychiatric disorders, this system becomes dysregulated, resulting in the loss of that essential coordination. Our innovation lies in aiming upstream, targeting the ECS to reinstate its regulatory role. By doing so, we hope to re-establish the conditions in which the brain's own circuitry can function in balance. This represents a fundamental shift in perspective; rather than attempting to correct each individual disruption, we aim to restore the conductor so that the orchestra, as a whole, can play in tune once again.

We aim to achieve this through a new mode of action we call Selective Endocannabinoid Reuptake Inhibitors (SERIs), an upstream intervention targeting the ECS which plays a central modulatory role across a wide range of mental health conditions.

What distinguishes your lead candidate, SYT-510, and how are you designing its development pathway to maximise clinical insight?

Our clinical development strategy for SYT-510 is shaped by the nature of the SERI mode of action. Rather than committing prematurely to a single indication, we are taking a stepwise approach that allows us to evaluate our lead candidate SYT-510 across symptom domains that cut across traditional diagnostic boundaries. These include anxiety, fear, repetitive behaviours, movement disorders, circadian rhythm disruptions, seizures, and potentially even neuroinflammatory and pain-related conditions. The aim is not to address all these complexities at once, but to identify where the most pronounced effects are observed and to prioritise those domains for subsequent

development. This will be done through a series of focused Phase IIa studies in well-defined patient populations. By exploring specific symptoms rather than fixed disease categories, we hope to build a more nuanced and data-driven rationale for later-stage trials.

Our Phase I trial, conducted in healthy volunteers, has already delivered several encouraging outcomes. SYT-510 has demonstrated a favourable safety and tolerability profile across both single and multiple ascending dose cohorts, with approximately 60 individuals dosed. The compound achieves plasma concentrations that align with pharmacologically active levels observed in preclinical models, and its pharmacokinetics are consistent with our expectations. Critically, we have confirmed brain penetration by measuring the presence of the compound in cerebrospinal fluid, a step not typically included in early-phase trials but one that provides important qualitative evidence of central activity. In addition, we have begun to observe exploratory pharmacodynamic signals suggesting a potential effect on brain function, although these data remain early and are subject to confidentiality constraints.

What distinguishes SYT-510 is its self-limiting, competitive, and reversible mode of action. In a normally functioning ECS, it does not perturb physiological balance. However, in the presence of dysregulation – whether excessive or deficient – it appears to exert a pro-homeostatic effect, restoring equilibrium without overstimulation. This has been consistently observed in our non-clinical studies and now begins to be reflected in early human data. Altogether, these findings give us a strong foundation for moving into targeted Phase IIa studies, where we can assess real-world clinical impact in specific symptom domains before scaling to larger, more resource-intensive trials. It is a deliberate and data-informed approach to building confidence in both the mechanism and the therapeutic potential of our lead compound.

Where do you see the most important inflection points as SYT-510 progresses toward broader clinical validation?

Although Phase I is typically considered a standard step in clinical development, completing it for SYT-510 represents a pivotal achievement for Synendos. This compound is not only our lead candidate but also the first molecule of SERIs to be administered in humans. We are, in essence, entering uncharted clinical territory. While preclinical models can provide valuable insights, they cannot fully replicate the complexity of human physiopathology, and demonstrating safety, tolerability, and brain penetration in healthy volunteers is a critical milestone.

The focus now shifts to evaluating the compound in patient populations. Rather than advancing directly into a single large indication, we are pursuing a symptom-domain-driven strategy. Many neuropsychiatric conditions share overlapping symptoms such as anxiety, compulsive behaviours, sleep disruption, and seizures. By targeting these domains specifically, we can identify where our approach delivers the clearest therapeutic signal. This stepwise model allows us to expand selectively and with greater precision.

We will begin with anxiety and fear-related symptoms, which are supported by robust preclinical evidence and validated translational paradigms. The study will assess SYT-510 in individuals presenting with anxiety traits over a defined treatment period, using both behavioural and imaging endpoints. We plan to initiate additional studies in domains such as movement disorders, seizure-related symptoms, and circadian rhythm disturbances.

Our objective over the next two to three years is to generate proof-of-mechanism, or ideally early proof-of-concept, in one or more of these symptom clusters to accelerate the path forward for a more focused and larger Phase IIb trial, potentially in conditions such as post-traumatic stress disorder (PTSD), generalised anxiety disorder (GAD), and obsessive-compulsive disorder (OCD). This measured, data-driven approach is designed to reduce clinical risk while allowing us to build a compelling case for broader development grounded in early human evidence.

What has been your approach to securing funding while ensuring both sustainability and strategic flexibility?

From the outset, we have adopted a deliberately balanced funding approach, combining both private investment and non-dilutive capital to support the company’s growth while maintaining strategic flexibility. Even before Synendos was formally incorporated, we were able to raise between CHF 700,000 and 800,000 in non-dilutive funding from a variety of sources; among them the European Union, Swiss accelerators, Innosuisse, BaseLaunch, Venture Kick, and private foundations.

That early support gave us a solid operational runway without immediately diluting the company’s equity. In 2020, we secured CHF 20 million in a Series A financing round, bypassing a traditional seed round. This was later extended to CHF 24 million in 2021 and has been instrumental in supporting our key development goals: confirming SYT-510 as a clinical candidate, completing all non-clinical and formulation work, advancing the compound into first-in-human studies, and demonstrating safety, tolerability, and brain penetration in Phase I. These were essential

milestones and positioned us to transition into clinical proof-of-mechanism with a strong foundation. Alongside this, we have continued to attract non-dilutive capital, securing an additional CHF seven to eight million over the past several years through programmes such as Eurostars and a substantial Innosuisse startup grant, each contributing around CHF three million. While these funds are extremely valuable, they play a supporting role; to execute our broader clinical strategy, we rely primarily on equity financing.

We are now in the process of raising a Series B round which will allow us to initiate multiple Phase IIa studies, each targeting a distinct symptom domain. By diversifying our clinical portfolio in this way, we can manage development risk more effectively and increase the overall probability of success. However, our strategy remains modular and can be scaled according to the capital available. Our focus is on maintaining optionality, ensuring that we continue to deliver data, and positioning the company to expand its clinical reach based on results, investor appetite, and market dynamics.

What dynamics are shaping investor and industry interest in neuroscience today, and how are you navigating that landscape?

There is no doubt that neuroscience is regaining prominence within the pharmaceutical and investment landscapes. Over the past few years, several major pharmaceutical companies have re-entered or strengthened their presence in this space. This renewed engagement has created a ripple effect, shaping perceptions within the venture capital community and signalling that the field is once again considered both strategically relevant and scientifically credible.

That momentum, however, does not erase the inherent complexity of neuropsychiatry, which continues to pose challenges for investors. For example, unlike other disease areas– where early-stage trials often benefit from measurable, biomarker-driven endpoints – psychiatric disorders typically rely on symptom-based assessments that are more difficult to standardise and interpret in an early stage. However, the availability and incremental incorporation of validated tools such as imaging techniques, EEG, wearables and the application of artificial intelligence algorithms provide a positive outlook into more accurate diagnosis, patient stratification and an early detection of treatment effects.

In fact, a further complication lies in diagnosis itself. Disorders like PTSD, GAD, or OCD are defined by symptom clusters, not underlying biology. As a result, patients with the same diagnosis may have widely different underlying biological profiles, introducing heterogeneity into trials and

complicating the detection of clear treatment effects. At Synendos, we are actively working to address this by integrating patient stratification approaches and objective, data-rich methodologies to enhance signal resolution and reduce variability.

Despite these challenges, the unmet need in neuropsychiatry is profound, and that reality is increasingly reflected in investor sentiment. While oncology remains a dominant focus, many investors acknowledge a degree of saturation and are looking toward the central nervous system (CNS) space as a logical next frontier. Still, familiarity with the field plays a significant role. While many venture funds describe themselves as therapeutic area agnostic, those with existing CNS expertise are generally quicker to engage, while others may approach with greater caution, which is entirely understandable.

As a company operating in this space, we see it as our responsibility not only to communicate the promise of what we are building, but also to be transparent about the risks and complexities involved. Our intention is not to oversell, but to demonstrate why our scientific rationale, our development model, and our data-driven approach offer a differentiated and credible path forward in a field where patients, clinicians, and systems alike are urgently seeking new options.

How are you building and evolving the Synendos team to meet the demands of a growing clinical pipeline?

While Synendos currently comprises ten full-time employees, the team driving daily execution is significantly broader. Including specialised consultants, many of whom participate regularly in strategic and operational discussions, we function as an integrated group of approximately twenty. These external contributors are not peripheral; they form a vital part of what I would consider our extended core team. This flexible, modular structure has served us well in early development, allowing us to access deep expertise across key functions such as medical affairs, clinical pharmacology, toxicology, and regulatory affairs, without incurring the structural weight of a larger organisation. However, as our pipeline advances and clinical activities intensify, the nature of our needs is changing. When a function shifts from being intermittently required to continuously engaged, internalisation becomes not only logical but necessary. We are now in that transition and are actively strengthening our internal clinical capabilities to reflect it.

Beyond clinical development, we are also focusing on bolstering project management, where strong individuals have brought us far, but the demands are now exceeding existing capacity. Coordinating across areas such as CMC, clinical and non-clinical development, logistics, and

operations requires not just technical oversight but structured, cross-functional leadership. This is particularly important in our model, where all core execution is outsourced. In the early days, we expected outsourcing to simplify operations, but in reality, it has demanded greater internal clarity and oversight. Our data, generated externally, constitute our core asset. Ensuring that our partners, whether CROs or other collaborators, align with our standards and execute accordingly requires careful planning, close interaction, and sustained engagement. It is, in many ways, more resource-intensive than in-house execution.

As we move into a more operationally complex phase, managing multiple clinical studies across diverse symptom domains, our focus is not on scaling indiscriminately, but on reinforcing the structure and capacity necessary to manage these activities with precision. We remain committed to maintaining the agility that has characterised Synendos to date, while evolving the team to meet the requirements of our next stage of growth.

What closing thoughts would you share with potential investors and industry stakeholders?

If there is one message I would emphasise, it is the importance of embracing genuine innovation, not just in principle, but in practice. While the term “innovation” is used widely and often enthusiastically, there remains a tendency across the industry to gravitate toward approaches that feel familiar or validated. In reality, meaningful progress often requires stepping beyond that comfort zone. At Synendos, we are developing a first-in-class mechanism without direct clinical precedent. Naturally, that places us in a more uncharted space, but it also opens up significant opportunity.

Our goal is not to disrupt convention for its own sake, but to introduce a novel therapeutic paradigm underpinned by a clear scientific rationale and advanced through a careful, data-informed strategy. In our view, innovation must be taken on its own terms; bold, but rigorously conceived. When approached with discipline and conviction, it does not inherently carry more risk than traditional paths; in some cases, it may even offer a clearer rationale and stronger long-term potential.

What experience has taught me is that predictability in this field is an illusion. Even compounds that follow seemingly well-validated models can fail in translation. One recent example involves muscarinic receptor modulators: while Karuna Therapeutics successfully advanced its candidate, a similar programme at Cerevel, built on the same concept, did not. Subtle differences in design or

execution can be critical. This reinforces the view that repeating what has worked elsewhere is no guarantee of success, nor should novelty be treated as inherently more precarious.

Ultimately, I believe this is a moment that calls for thoughtful boldness. The need in neuropsychiatry is urgent, and we have the scientific tools to pursue fundamentally new solutions. For investors and partners, the opportunity lies in supporting innovation that is not only distinctive, but also grounded in scientific rigour and strategic clarity. That is the path we are following at Synendos: not chasing novelty for its own sake, but building something different because the science and the patients demand it.

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