Nuno Sousa – President, 2CA-Braga

A collaborative environment … can potentially position Portugal on par with Spain in the clinical research landscape within the next five years

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Nuno Sousa details the development of Portugal's clinical research ecosystem, highlighting the creation of the Clinical Academic Center of Braga (2CA-Braga) and its evolution. He emphasises the necessity of building on 2CA Braga's successes to create a network of strong research centres across Portugal, making the country a more competitive destination for clinical trials in Europe.

Could you provide a brief overview of yourself and the various roles you hold in the clinical development sector in Portugal?

I hold an MD degree with a background in neuroradiology. My work spans fundamental neuroscience research to clinically oriented studies. Until a year and a half ago, I served as the medical school's dean at the University of Minho, which I co-founded 22 years ago. During my tenure, we established a cluster, and one of its key pillars focused on education, while another centred around research. We initiated the Biomedical Research Institute and recognized the importance of having a clinical research facility, leading to the establishment of the Clinical Academic Center of Braga (2CA-Braga) in 2012, located just across the street. The remaining pillars are value sustainability, including an association dedicated to IP protection, and tech transfer. Lastly, we introduced a Clinical Digital Centre which I oversee, providing patient care through digital tools. I have recently transitioned from the role of dean to become the president of 2CA.

Could you shed some light on how well Portugal performs in terms of the fundamental elements required to build a clinical development ecosystem: critical mass, science, and funding?

These are indeed the foundational elements for a successful project. Our journey began with the establishment of the medical school 22 years ago, at a time when Portugal only had public medical schools, with one private exception. The Portuguese government recognized the need for innovation in medical education and sanctioned the creation of our medical school. We focused on innovating medical education, achieving significant success, and earning prestige both nationally and internationally. Subsequently, realizing that a good medical school must be complemented by robust research, we initiated the Biomedical Research Institute. At that time, the national ecosystem was more developed in the biomedical research dimension than in clinical research.

Despite considerable growth in translational and clinical research, it was evident that clinical research was lagging behind due to a lack of infrastructure, specifically dedicated personnel, autonomous management, and committed researchers. To address this, we embarked on an unconventional approach. The Portuguese government decided that Braga’s hospital, a significant public hospital, would operate under a public-private partnership, and clinical management was entrusted to the private partner, between 2009 and 2019. This decision allowed us to establish a Clinical Research Centre as part of a public-private non-profit association, providing flexibility in management. With this framework, we transitioned from having almost no clinical trials to conducting over 250 clinical studies, recruiting more than 1000 participants, and employing over 30 full-time professionals dedicated to clinical research. As an academic CRO, we offer sophisticated clinical services and serve as the backbone for a robust clinical research program.

This approach has yielded impressive results, with rapid recruitment, feasibility responses within 24 hours, recruitment rates consistently above 100 percent, and the first patient recruited in less than 15 days. This success has fostered trust among promoters, CROs, researchers, and patients, positioning us as one of the top centres in Portugal, competitive in the European landscape. However, the challenge lies in expanding further. A single centre, no matter how strong, might not attract complex trials from major pharmaceutical companies. Therefore, our focus is on replicating this success and building a network for greater impact.

Are the 250 trials you mentioned a mix of investigator-led trials and those requested by sponsors? Additionally, what are the disease areas where you have a stronger focus,

considering your background in neurology and the challenges associated with this complex area?

Regarding the portfolio of clinical trials, approximately half of the studies are classical trials. In contrast, the other half comprises non-classical trials, including observational studies, real-world evidence studies, and pragmatic clinical trials. About 90 percent of these trials are sponsored by industry, with a smaller percentage led by researchers. In terms of clinical trial phases, around 10 percent are phase 1, 10-15 percent are phase 2, and the majority are phase 3. The decision to have minimal phase 4 trials was intentional.

As for disease areas, the portfolio aligns with typical European centres, with a predominant focus on oncology and neurology. Following these, there is a broad spectrum of studies in neuroscience, metabolic disorders, and cardiovascular diseases, reflecting the common profile observed in clinical trials across the continent.

How many hospitals in Portugal can potentially be connected to the clinical trial network, considering the need for critical mass? Additionally, could you explain the regulatory alignment and approval process across different hospitals in Portugal compared to the challenges faced in some European countries with regional variations?

In Portugal, our clinical trial network operates within a national system, which simplifies the regulatory alignment and approval process. Unlike some European countries with regional variations, we don’t encounter the challenge of having to redo protocols when moving between hospitals. The national system allows for a streamlined approach, eliminating unnecessary costs and bureaucracy associated with regional disparities. While there are five regions for primary care approvals, for our clinical trial network, we benefit from a more cohesive and efficient national framework.

Could you provide insights into the discussions and progress regarding unifying a connected clinical trial network beyond your centre in Braga? What objectives are being pursued?

The discussions about unifying a connected clinical trial network beyond our centre in Braga are in progress at a national level. The objective is to enhance the autonomy of clinical research centres in Portugal. The current model, where research centres operate as departments within hospitals,

lacks the agility needed to meet the deadlines set by clinical research promoters. The goal is to create more flexibility in management and establish a one-stop entry system that facilitates collaboration between different healthcare institutions. While this initiative is still in the conceptual stage, the aim is to replicate successful models implemented by other countries, such as Spain, with the potential to significantly impact and elevate the entire clinical research system in Portugal.

What is the realistic potential for Portugal as a clinical trials destination and, when representing your centre to major sponsors, what compelling selling points do you offer?

In the current landscape, especially post-COVID, governments recognize the value of biomedical research, acknowledging its pivotal role in addressing healthcare challenges. For a relatively small country like Portugal, standing out is indeed a challenge, especially when compared to the success of larger counterparts like Spain. However, when I approach major sponsors, the key lies in showcasing the outstanding performance metrics of our clinical research centre. By presenting compelling Key Performance Indicators (KPIs), such as our world-leading efficiency, we establish our centre as highly competitive.

During these presentations, sponsors often remark on the excellence we demonstrate. I humorously acknowledge their scepticism, assuring them that our data is genuine. We pride ourselves on efficiency, illustrated by the fact that 52 percent of our feasibilities are converted. The remaining 48 percent typically results from Portugal not being the chosen location, a factor beyond our control.

To attract sponsors effectively, the crucial selling point is not just the excellence of a single centre but the vision of creating a network of strong research centres across Portugal. Rather than aiming for one or two, the objective is to have four, five, or six robust centres that collectively form a powerful ecosystem. This strategy aligns with my role as the head of this research centre, where I emphasize the need for multiple centres to ensure substantial recruitment capabilities.

Our centre’s success story serves as an inspiration for other research centres, with three or four already attempting to replicate our model. Leveraging the experience and with the support of initiatives promoted by AICIB (The Portuguese Agency for Clinical Research), efforts are directed towards creating standardized rules and licensing conditions. The goal is to empower these emerging centres to achieve a similar position, fostering a collaborative environment that can potentially position Portugal on par with Spain in the clinical research landscape within the next

five years. My intimate knowledge of the Spanish ecosystem, gained through my involvement in scientific boards of hospitals, underscores the importance of fostering an entire network of strong centres, as passive centres may not contribute to the transformative wave needed to elevate Portugal's standing.

Do you think countries like Portugal, with lower labour costs, could potentially have a competitive advantage in attracting clinical trials? Also, pharmaceutical industry professionals have expressed concerns about a potential decline in clinical trials if market approval is not secured. What is your take on that?

Your observation about the perceived inertia in initiating clinical trials due to existing market access and approvals for innovative medicines is thought-provoking. As you rightly pointed out, establishing a clear and direct correlation between market authorization and the initiation of clinical trials remains a challenge. When pressed for this connection, responses from industry professionals have been evasive, and a definitive link seems hard to pinpoint.

Interestingly, your perspective introduces the idea that countries like Portugal, with lower labour costs, could present a competitive advantage. However, the emphasis on adherence to the European ecosystem's highly regulated standards, rather than cost considerations, seems to be a more compelling narrative. Trust is instilled among promoters, whether they are major pharmaceutical companies or startups, due to Portugal's commitment to regulatory excellence.

In my experience, this approach has led to numerous companies worldwide approaching us for collaboration, particularly for early-phase studies. While cost is a factor, it often takes a back seat for startups, with the regulatory environment taking precedence. Thus, rather than leading with the notion of being cheaper, we highlight Portugal's position within the well-regulated European system as a key selling point. This has proven effective in attracting a diverse range of companies seeking to develop their studies, including phase 1 and phase 2 studies.

Considering Portugal's geographical location, there may be biases and challenges to overcome. **However, you've emphasized the need for Portugal to rise to the highest international standards. How do you navigate these challenges, and in what ways does your center strive to compare itself not just nationally but with the best centres in Europe?**

Indeed, Portugal faces unique challenges due to its geographical location, being both at the periphery and in Southern Europe. While these biases are real, we must overcome them by raising our standards to meet the best international benchmarks. In my role at the centre, I've adopted a mindset of not comparing ourselves merely at the national level but aspiring to be on par with the very best centres in Europe. This approach isn't about winning a national championship but striving to learn and excel by competing with the best in the broader European landscape. The recent challenges with the government underscore the need for us to continually prove our commitment to elevated standards.

The focus isn't solely on economic improvements; rather, it's about enhancing healthcare standards and ensuring patients have access to cutting-edge interventions. By aligning with European platforms for study registration and collaborating with regulatory authorities, we are playing an active role in shaping a robust clinical research landscape. This not only contributes to economic advancement but, more importantly, allows patients in Portugal to access innovative treatments that might otherwise be unavailable. The overarching goal is to provide better healthcare and bridge the gap between geographical biases and the delivery of top-tier medical interventions.

Can you elaborate on how you navigate the varying levels of expertise among clinicians in your centre and the role of clear and transparent rules in promoting excellence?

Certainly, when we discuss competitiveness in the European landscape, it brings forth an increased responsibility for clinicians. The emphasis is not only on their clinical proficiency but also on visibility at the European level. I firmly believe that the distribution of quality and intelligence is normal, and like any institution, we have a mix of clinicians with varying capabilities. However, what sets us apart is our ability to establish clear and transparent rules, enabling us to promote the very best in our team.

In my experience, I've encountered challenges in other places in Portugal when attempting to conduct clinical trials due to cumbersome bureaucratic processes. Now, within our centre, clinicians need only focus on running excellent clinical trials, as the administrative hurdles have been significantly reduced. This streamlined approach allows them to confidently assert our competitiveness on the European stage.

One crucial factor in our competitiveness is the backstage infrastructure. We excel in specific areas, such as clinical neurosciences, imaging, and the associated infrastructure like imaging

biobanks. This specialization allows us to stand out and compete effectively in these domains. However, it’s essential to recognize that competitiveness can vary across different areas, and our ability to compete is contingent on having the necessary top-notch infrastructure, particularly in those areas where we aim to excel. This holistic approach, combining clinical expertise, streamlined processes, and robust infrastructure, positions us to be competitive and contribute significantly to the European clinical research landscape.

In the context of global clinical trials, especially involving biotechs, how do you see the opportunity for European centres, given the current challenges with FDA approvals and the bias of certain biotechs toward North America?

The opportunity for European centres to engage with global biotechs is a mixed bag. On one hand, there is a bias among certain biotechs to focus solely on North America, prioritizing FDA approvals. This bias can be challenging to overcome, and currently, Europe might not be on the map for these biotechs. However, it’s more of a mental bias than a fundamental limitation. As Europeans, there’s a collective need to promote the capabilities of European centres and demonstrate that they can effectively contribute to global multicenter trials. While challenging, it’s not impossible to shift this bias.

There are specific regions where European centres can find opportunities. While there may be challenges in engaging with certain biotechs from Asia, opportunities exist in South America and Africa. These markets, while substantial, are not as well-developed in terms of clinical research. If approached strategically and with a focus on niche opportunities, European centres, including those in Portugal, can establish fruitful partnerships. For example, being Portuguese provides significant opportunities in countries like Brazil, which is a large pharmaceutical market.

Any final thoughts or advice for investors involved in clinical trials?

My parting advice for investors deeply engaged in clinical trials would be to embrace impartiality. It’s crucial to maintain an open mind and venture into opportunities beyond preconceived notions. Avoid restricting considerations to specific regions or biases; instead, foster openness towards partnerships and collaborations that could provide distinctive advantages within the global clinical trial landscape. In this dynamic field, flexibility and a willingness to explore diverse avenues can lead to valuable insights and opportunities that might otherwise be overlooked.

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