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Targeting Cortisol: The Hidden Driver Behind Difficult-to-Control Type 2 Diabetes

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At BIO 2026, Robert Jacks, CEO & President of Sparrow Pharmaceuticals, discusses how cortisol modulation could unlock a new treatment paradigm for patients struggling with diabetes, obesity, hypertension, and broader cardiometabolic disease.

As the global burden of cardiometabolic disease continues to rise, researchers are increasingly looking beyond traditional treatment approaches to uncover the biological drivers that leave millions of patients inadequately controlled despite existing therapies. **At BIO International Convention 2026 in San Diego, BioSpectrum Asia spoke with Robert Jacks, CEO & President of Sparrow Pharmaceuticals,** about the growing evidence linking excess cortisol to treatment-resistant type 2 diabetes and other metabolic disorders. He explains how Sparrow's novel cortisol-modulating approach could redefine patient stratification, complement current diabetes and obesity therapies, and create an entirely new category of precision medicine for cardiometabolic disease.

What role does cortisol play in cardiometabolic disease?

Cortisol is a glucocorticoid hormone that plays a central role in regulating a wide range of metabolic processes including glucose metabolism, blood pressure, lipid levels, weight, and even sleep and mood. At normal levels, cortisol contributes to glucose homeostasis in multiple ways. However, when chronically elevated, cortisol acts across different organ system pathways to decrease insulin production, increase insulin resistance, and increase glucogenesis, causing a disruption to nearly every one of those pathways simultaneously. This spectrum of dysfunction can cause or exacerbate type 2 diabetes (T2D) and can render currently approved therapies less effective and ultimately contribute to broader cardiometabolic disease.

What we've come to understand based on growing scientific evidence over the past couple of decades is that there is a meaningful subset of patients with difficult-to-control cardiometabolic diseases like T2D and hypertension whose underlying condition is being silently driven by excess cortisol. They're not responding to standard therapies because the treatments are addressing downstream consequences rather than the upstream driver.

The most vivid illustration of this comes from our own clinical data. Interim Part 1 results from our CAPTAIN-T2D study (NCT07296484) show that more than 75% of patients with difficult-to-control type 2 diabetes have elevated cortisol levels associated with increased cardiovascular risk. These patients struggle to control their blood glucose, blood pressure, weight, and lipids, and they often experience resistance to current agents. What the data are telling us is that excess cortisol is a common, underappreciated upstream driver of difficult-to-control cardiometabolic disease: present, undiagnosed, and in a much broader population than previously recognized.

Could targeted cortisol modulation become a major new treatment category?

HSD-1 inhibitors, which work by regulating intracellular cortisol levels, were originally developed for metabolic diseases, such as diabetes, and demonstrated efficacy and a clean safety profile. They simply weren't sufficiently differentiated when applied broadly to the general diabetic population. The mechanism was sound; the patient selection was too wide.

What's changed is our ability to identify the right patients: those who show elevated cortisol risk as a true underlying driver of their difficulty in controlling their disease state. Our interim CAPTAIN-T2D data are a significant step forward here. Among nearly 400 patients screened with difficult-to-control T2D, more than three-quarters had elevated cortisol at levels associated with increased cardiometabolic risk — and importantly, these patients are straightforward to identify. Patients with inadequately controlled T2D who also had hypertension or were using an incretin agonist were more likely to have higher cortisol levels, giving clinicians a clear and accessible profile to work from. That transforms what was previously a plausible hypothesis into an actionable clinical and commercial opportunity.

If you can reliably identify patients whose cardiometabolic disease is being driven by undiagnosed cortisol excess, and you have an agent that modulates that mechanism effectively and safely, that is the foundation for a genuinely new and important treatment category. Given the scale of this patient population, the impact could be substantial.

How does your approach complement existing diabetes and obesity therapies?

An important framing is that clofutriben is not intended to replace existing therapies, but to help explain why those therapies may not be working for a specific group of patients and then address that underlying root cause.

Clofutriben is a novel HSD-1 inhibitor designed to selectively reduce intracellular cortisol in key metabolic tissues, targeting a long-recognized biological driver of poor glucose control and treatment resistance in some patients with T2D and cardiometabolic disease. Its mechanism of action is complementary to GLP-1 agonists and insulin sensitizers, offering a new approach for patients who remain uncontrolled on current regimens and a more targeted way to treat cortisol-driven metabolic dysfunction.

The standard of care in T2D is excellent for many patients, and the GLP-1 receptor agonist class in particular has been transformative. But there remains a meaningful population of patients who do not respond adequately, even to the best available treatments. That difficult-to-control disease represents a real and largely unaddressed clinical problem.

In many of those cases, we believe underlying cortisol excess may be creating a metabolic headwind that conventional therapies cannot overcome because they were not designed to address it. Our approach is to target that upstream driver. In doing so, we are not competing with existing therapies; we are addressing a gap they leave. For patients whose disease is cortisol-driven, modulating that mechanism could potentially make them more responsive to their existing treatment regimens, which is why we think actively about the combination potential.

What patient populations stand to benefit most?

Cardiometabolic disease remains one of the greatest and fastest-growing global health crises, encompassing T2D, obesity, hypertension, and related cardiovascular conditions that together affect billions of people worldwide. Today, almost 1 billion adults live with obesity, over 800 million with diabetes, and nearly 1.4 billion with hypertension. Cortisol dysregulation cuts across all of these conditions, making it a compelling and underexplored therapeutic target.

Our first proof point is T2D, with near-term goals to expand into difficult-to-control hypertension and obesity. The clearest and most immediate beneficiaries are patients with difficult-to-control type 2 diabetes who have unrecognized elevated cortisol. These are patients who are failing current therapies not because the drugs don't work but because there's an underlying hormonal driver that's been missed. Estimates suggest this could represent several million people in the United States alone. These patients often feel like they're doing everything right and still can't control their disease, and that's a deeply frustrating and clinically serious situation.

Importantly, our program is structured to include patients with broader cardiometabolic dysfunction with difficult-to-control disease states. We see these populations as complementary, connected by the same underlying biology.

What are the next major milestones for the programme?

We're at a genuinely exciting inflection point. We've recently completed a successful financing round, which gives us the runway to execute on our key priorities, and the convergence of our clinical data with emerging scientific validation in the field has put us in a very strong position.

Our primary focus now is advancing our program in difficult-to-control type 2 diabetes with underlying cortisol excess, a population our CAPTAIN-T2D data confirm its far larger than many appreciated. The interim screening results we presented at ENDO 2026 validate both the prevalence of elevated cortisol in this population and the ability to identify these patients through readily available clinical markers. The next critical milestones will be completing enrollment and generating the Phase 2b treatment data that will demonstrate what happens when you address the cortisol driver directly in this population.

In parallel, we’re beginning to think carefully about pipeline expansion. Specifically, we will be identifying where else along the cardiometabolic spectrum this same cortisol-modulation mechanism could be applied. Difficult-to-control hypertension is an area of active interest, as are the other metabolic sequelae we know are linked to cortisol excess. We see a real opportunity to methodically extend our understanding of this mechanism into adjacent patient populations where the same underlying driver is at work.