December 6, 2025

Re: Application PDEV-19131

Dear Members of the Application Review Subcommittee,

I am a physician scientist who specializes in clinical urogynecology and reconstructive pelvic surgery. Since I began my clinical practice, I have been intrigued by the causes of urinary incontinence and also disturbed by the many patients who are afflicted by this very common and debilitating condition which is associated with poor quality of life, loss of productivity, and shame. While I helped these patients with existing treatment options, including surgery, a significant portion either saw no improvement or returned to my clinic later with recurrent incontinence.

This compelled me to devote the first decade of my career to investigating the cellular and molecular mechanisms associated with stress urinary incontinence. I discovered that this condition is associated with loss of smooth muscle cells and altered proteins, such as elastin, in the urethral sphincter. This led me to understand that the reason why existing therapies have limited long term efficacy is because they do not address these mechanisms. The solution is transplantation of rejuvenated smooth muscle cells into the urethral sphincter to replace lost cells and to restore a normal protein profile. The cells that could potentially carry out these complex tasks must possess regenerative and rejuvenated attributes since many of the patients who return to my clinic with recurrence are older and have failed all available treatments. Autologous iPSC-derived progenitor smooth muscle cells are the ideal candidate!

Urinary incontinence affects a large and diverse patient population with greater than two thirds of the burden being borne by women. Thus, the well-being and economic consequences have untold implications for women's health both in California and the United States. The GWG comments on our proposal accurately support this. The Reviewers recommended additional improvements in CMC areas. To ensure success, we have already addressed their recommendations by assembling a robust team with extensive CMC expertise, which includes the staff of the Stanford cGMP manufacturing facility. This team will engage the FDA on CMC requirements and incorporate their input throughout the project.

With continuous NIH and CIRM funding, my team has taken this project from its inception to completion of a pre-IND meeting with the FDA. A priority for CIRM 1.0 was to fund development of therapeutics for rare diseases. A goal of CIRM 2.0 is to support development of therapeutics that reach broader populations. Our project aligns perfectly with CIRM 2.0 and this cycle's PDEV funding will allow us to bring this treatment to patients without delays. Importantly, we already have potential partners in industry with a keen desire to partner with us for clinical trials once this therapy gains IND clearance.

We respectfully request the Subcommittee's support to fund this PDEV proposal which has a meaningful, direct impact on women's health.

Sincerely,

Bertha Chen, MD
Professor of Obstetrics & Gynecology
Professor of Urology (by courtesy)
Department of Obstetrics & Gynecology
Stanford University School of Medicine