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"KEGELS IN A BOTTLE": PRELIMINARY RESULTS OF A SELECTIVE ANDROGEN RECEPTOR MODULATOR (GTX-024) FOR THE TREATMENT OF STRESS URINARY INCONTINENCE IN POST-MENOPAUSAL WOMEN

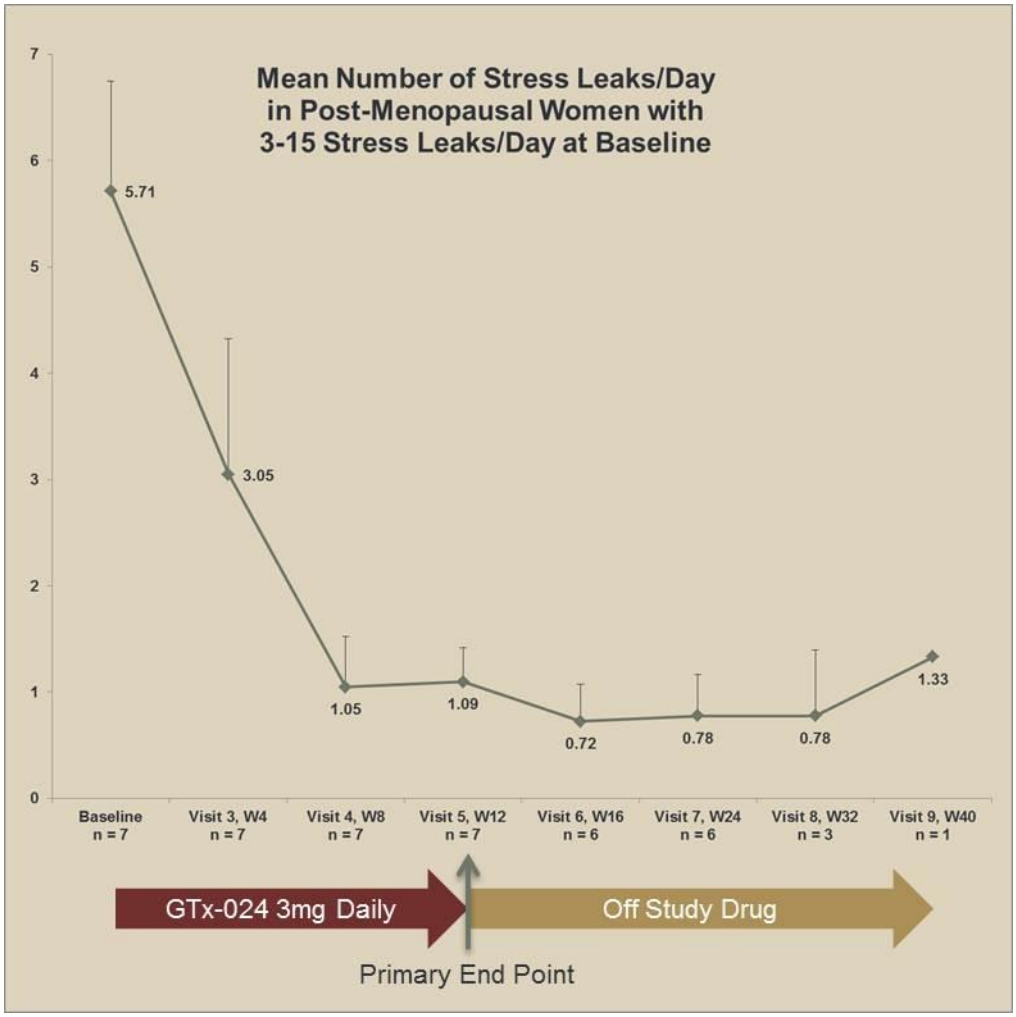
Hypothesis / aims of study
There are no effective oral therapies available in the US for women with stress urinary incontinence (SUI). The pelvic floor and urinary sphincter are androgen receptor (AR) rich and can be modulated by androgenic agents. GTx−024 is a novel selective AR modulator (SARM) that has been shown to be well tolerated in clinical trials of more than 1,500 patients for other disease processes. The purpose of this pilot study is to assess the efficacy and safety of GTx−024 for the management of SUI.

Study design, materials and methods
In this Phase 2 study, 3 mg of GTx−024 was given daily for 12 weeks to post−menopausal women. Inclusion criteria were predominant SUI, SUI symptoms for ≥ 6 months, 24 hour pad weights >3 grams, 3−15 SUI episodes per day averaged over three days, and a positive bladder stress test. The primary endpoint is the number of stress incontinence episodes per day on the 3-day voiding diary. Secondary endpoints include: pad weights, bladder stress test, and quality of life instruments including the Female Sexual Function Index (FSFI) and Patient Global Impression of improvement (PGI-I).

Results
This study is ongoing and the preliminary findings are presented on the first seven patients completing 12 weeks of treatment. Mean stress leaks decreased by 80.9% (Figure) and all patients saw at least a 65% reduction in leaking episodes. Stress leaks decreased from a mean number per day of 5.7 at baseline, to 1.1 at 12 weeks. Patients are being followed for durability of response post treatment and are demonstrating continued improvement up to 5 months. Patients pad weights decreased from a mean of 29.6 g at baseline, to 13.9 g at 12 weeks. FSFI scores increased from a mean of 16.8 at baseline, to 20.3 at 12 weeks, with 5/7 patients showing improvement. In all seven patients, PGI-I scores were improved at 12 weeks. Adverse events were minimal with none above a Grade I.

Interpretation of results
Both animal and human studies have demonstrated that a Selective Androgen Receptor Modulator can result in enhancement of muscle mass. The pelvic floor muscles are rich in androgen-receptors {1}. The role of the pelvic floor in maintaining the continence mechanism in women has been well established and is the basis of Kegel exercises and pelvic floor physical therapy. The integrity of the pelvic muscle support can be compromised by physical insults such as vaginal childbirth, atrophy associated with aging and changes in the hormone milleu. This is the first study to assess the role of a SARM in the management of SUI. The early results of this study showed an excellent safety profile with a profound effect on reducing incontinence episodes per day, improving quality of life and enhancing female sexual function. Interestingly, the improvements in symptom were sustained well beyond stopping the study drug. Although the results have been very impressive in this pilot study, the small sample size is a recognized limitation. A placebo-controlled trial is in development to further study the effect of GTx-024 in SUI.

Concluding message
These early results suggest GTx−024 substantially improves stress incontinence in women with associated reductions in pad weight and improvements in quality of life measurements. The safety profile has been excellent. Additional patients will be studied as part of this ongoing study.



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Disclosures

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