Title: **MYSTICOL: A randomized, controlled study of Myobloc in the treatment of sialorrhea for Amyotrophic Lateral Sclerosis (ALS) and neurological conditions.**

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**Background:** Uncontrolled sialorrhea (drooling) typically complicates diseases such as Amyotrophic Lateral Sclerosis (ALS) and Parkinson’s disease (PD) and can cause embarrassment, social isolation, perioral skin breakdown, and deterioration of dentition. RimabotulinumtoxinB, also known as Myobloc (MYO), has been reported to improve sialorrhea stemming from various causes including ALS and PD. We report on the largest controlled study of MYO in the treatment of sialorrhea due to ALS, PD and other etiologies.

**Methods:** Eligible patients presented with troublesome sialorrhea due to ALS, PD, Stroke, or other neurological conditions. Subjects were blindly and randomly assigned to receive either MYO 2500U total or MYO 3500U total or placebo. Subjects were followed for 13 weeks post-injection. Co-primary outcomes were: Unstimulated Salivary Flow Rate (USFR) and Clinical Global Impression of Change (CGI-C) at Week 4 post-injection compared to baseline. Multiple secondary outcomes were also collected as well as safety data.

**Results:** A total of 187 subjects were enrolled (safety population) and 184 subjects comprised the Intention-to-Treat (ITT) analysis group having received either 2500U MYO n=63; 3500U MYO n=64; or placebo n=57. Sialorrhea etiologies by percentage were: PD 65%, ALS 7%, Stroke 7%, other 21%. MYO injection sites were localized by anatomical landmarks in 75% and ultrasound (US) guidance was used in 25%. Both co-primary outcomes were significantly improved at week 4 compared to baseline pre-injection vs placebo: both USFR and CGI-C p<.0001 in both active treatment arms. Secondary analyses revealed significant improvement in both USFR and CGI-C at week 1 extending through week 8 post-injection in both active treatment groups with maintained improvement in the USFG only in the high dose group at the last observation point at week 13. Initial analyses as planned revealed no significant differences in outcomes based on injection technique using anatomical landmark vs US guidance. No unexpected side effects were reported.

**Conclusions:** MYO is effective for troublesome sialorrhea in ALS, PD and in other neurological conditions. Doses of both 2500U and 3500U are effective when injected into the parotid and submandibular glands; the higher dose may provide longer duration of benefit.