

# REVANCE THERAPEUTICS

## Abstract #1180:

### A PHASE 2, OPEN-LABEL, DOSE-ESCALATING STUDY TO EVALUATE THE SAFETY AND PRELIMINARY EFFICACY OF DAXIBOTULINUMTOXINA FOR INJECTION (RT002) IN ISOLATED CERVICAL DYSTONIA

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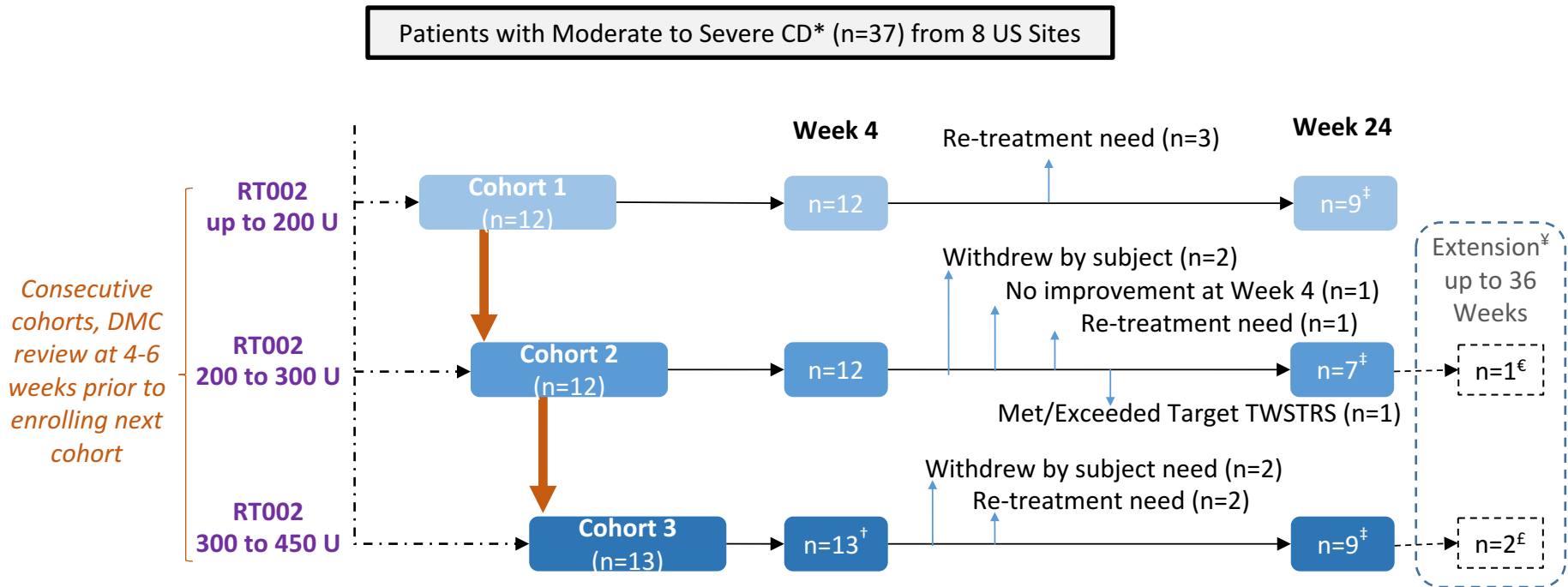
International Congress of Parkinson's Disease and Movement Disorders  
Vancouver, British Columbia  
8 June 2017



# Introduction

- Isolated cervical dystonia (CD) is a chronic neurologic disorder characterized by involuntary patterned contractions of cervical musculature resulting in abnormal movements or postural changes of the head, neck, and shoulders.
- Currently available treatments for CD call for injection of botulinum toxin (BoNT) about every 3-4 months, or 3-4 times per year.
- DaxibotulinumtoxinA for Injection (RT002), a neuromodulator currently in clinical development, is comprised of a 150 kDa BoNT-A molecule and a proprietary peptide, with no animal-derived components or human serum albumin (HSA).
- Study Objectives:
  - To assess the safety and preliminary efficacy of RT002 for Injection in subjects with isolated CD
  - To evaluate the duration of effect of RT002 for Injection in the treatment of isolated CD

# Dose-Escalating Study Design and Subject Disposition



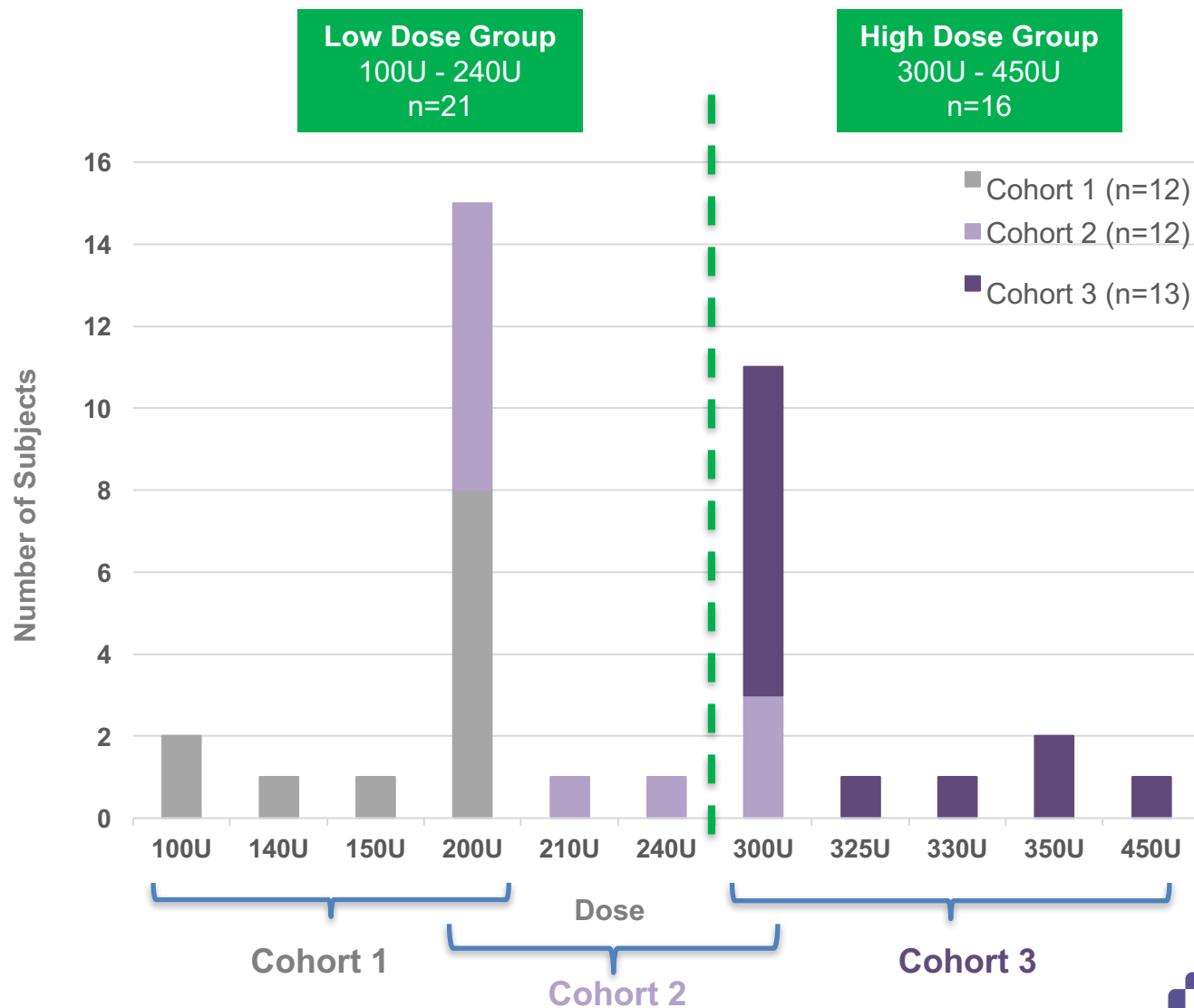
Subjects were evaluated at 2-4 week intervals for 24-36 weeks or until loss of benefit.

\*TWSTRS-Total  $\geq 20$ , TWSTRS-Severity  $\geq 15$ , and treatment-naïve or no BoNT within last 6 months.

<sup>†</sup>Two subjects missed the Week 4 visit. <sup>‡</sup>Met/exceeded Target-TWSTRS at Week 24 for n=1 in Cohort 1 and n=2 in Cohort 2; at Week 20 for n=2 in Cohort 2; at Week 6 for n=1 in Cohort 3. <sup>¥</sup>Added in the protocol as of January 2017.

<sup>£</sup>Completed Week 36. <sup>€</sup>Ongoing.

# Subject Distribution by Dose



# Demographics and Baseline Characteristics

## By Dose Group

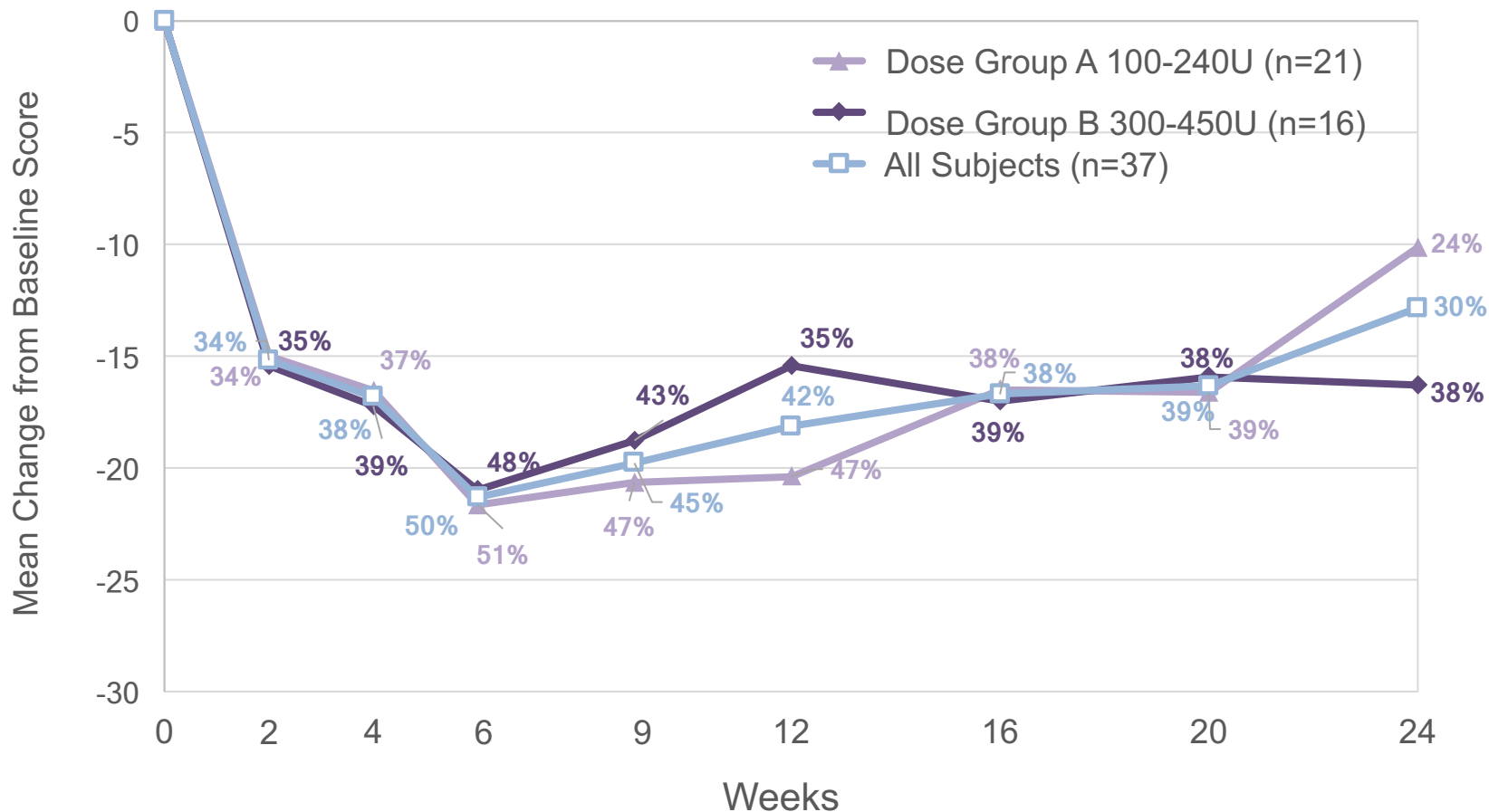
	<b>Group A</b> 100-240 U (n=21)	<b>Group B</b> 300-450 U (n=16)	<b>All</b> (n=37)
<b>Mean age</b> [range]	54 [32–74]	58 [30–70]	56 [30–74]
<b>Females, n (%)</b>	18 (86%)	10 (63%)	28 (76%)
<b>Caucasians, n (%)</b>	18 (86%)	14 (88%)	32 (86%)
<b>Mean/Median CD duration (yrs)</b> [range]	7.3/4.8 [0.02–24.1]	7.9/7.2 [0.02–23.3]	7.6/4.9 [0.0–24.1]
<b>Prior treatment with BoNT</b>	9 (43%)	8 (50%)*	17 (46%)
<b>Mean RT002 dose, U</b>	188	319	244
<b>Mean TWSTRS Score:</b>			
<b>Total Score</b>	44.4	43.8	44.1
<b>Severity Score</b>	20.5	21.9	21.1
<b>Disability Score</b>	12.6	11.6	12.2
<b>Pain Score</b>	11.3	10.3	10.8

\*Three subjects received RT002 in Cohort 1 or 2, and re-enrolled to Cohort 3.

# Reduction in TWSTRS-Total Score Over Time

## By Dose Group

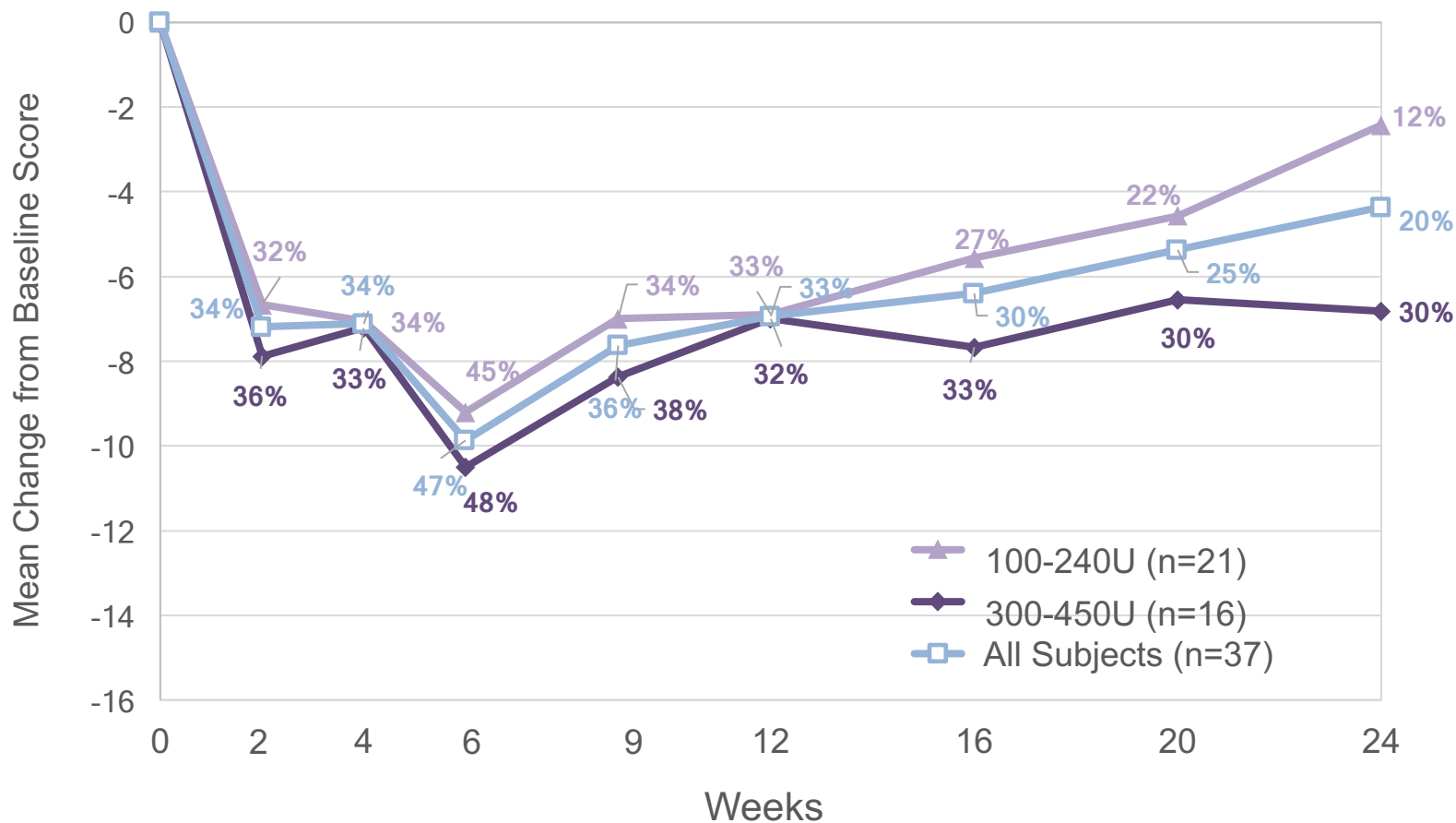
Clinically meaningful reduction in TWSTRS-Total Score of 34% for all subjects beginning at Week 2, with the majority of this benefit maintained through Week 24 in both dose groups



# Reduction in TWSTRS-Severity Over Time

## By Dose Group

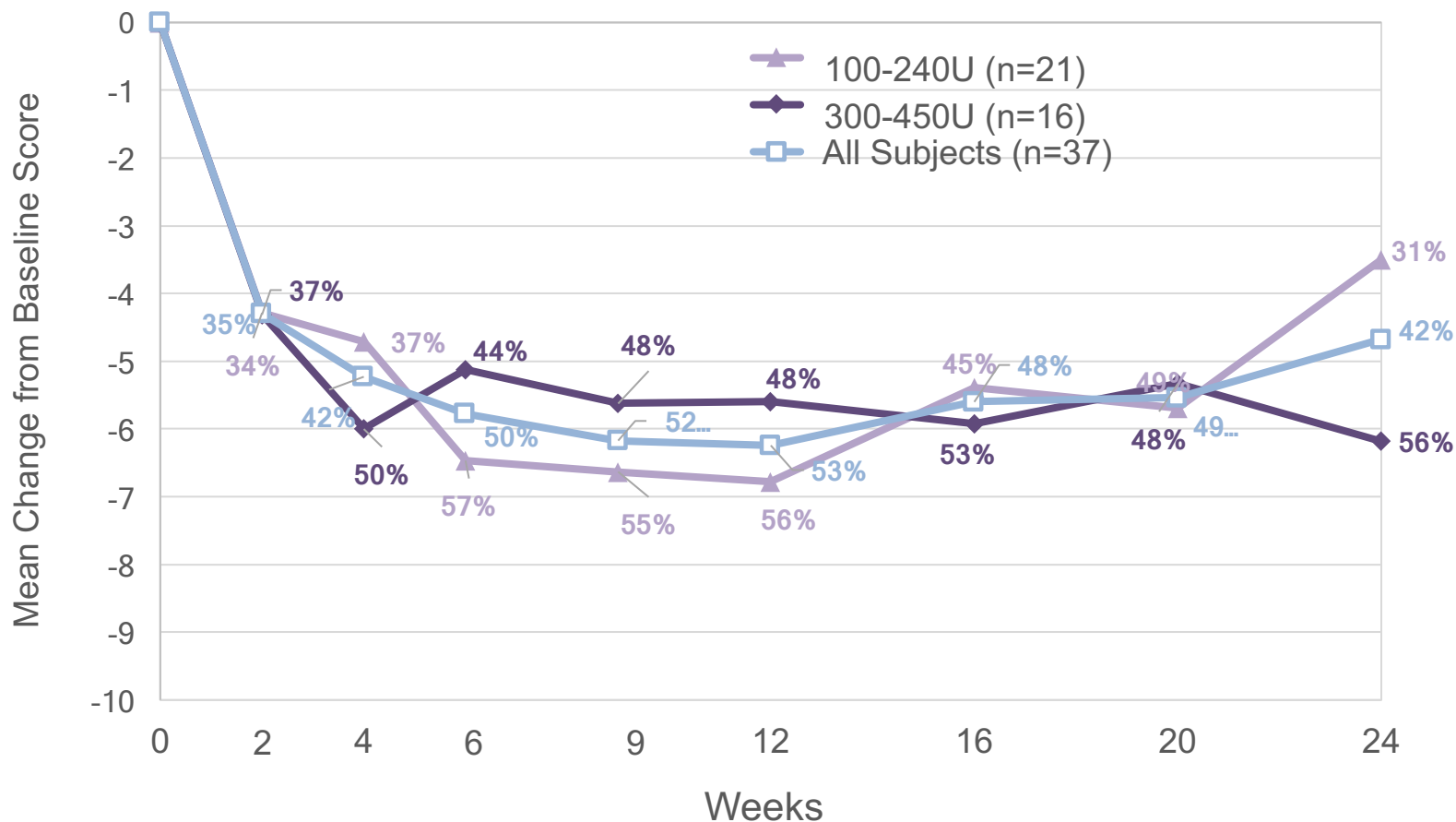
Clinically meaningful reduction in TWSTRS-Severity Score of 34% for all subjects beginning at Week 2, with the majority of this benefit maintained through Week 24 in both dose groups



# Reduction in TWSTRS-Disability Over Time

## By Dose Group

Clinically meaningful reduction in TWSTRS-Disability Score of 35% for all subjects beginning at Week 2, with the majority of this benefit maintained through Week 24 in both dose groups

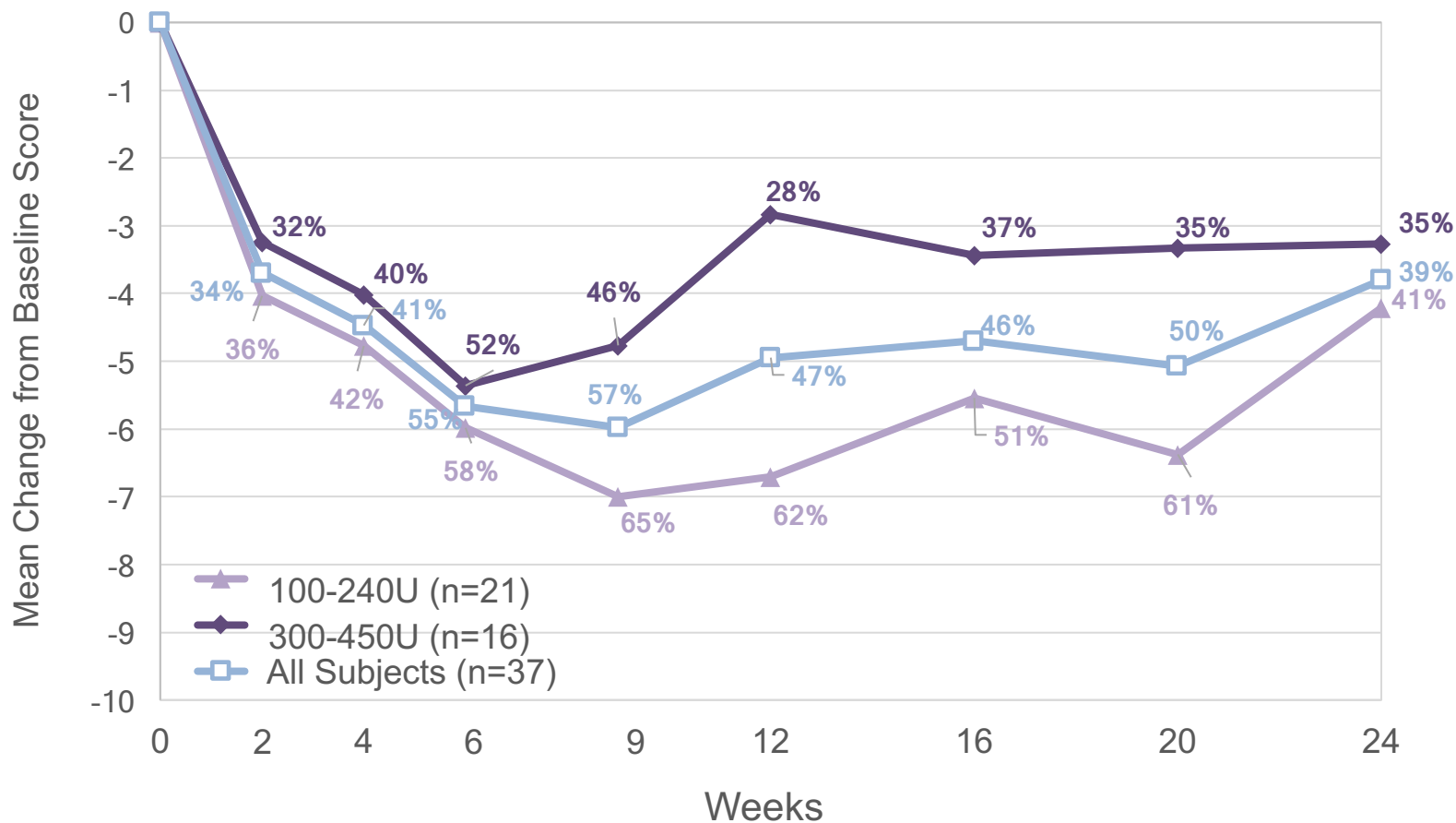




# Reduction in TWSTRS-Pain Over Time

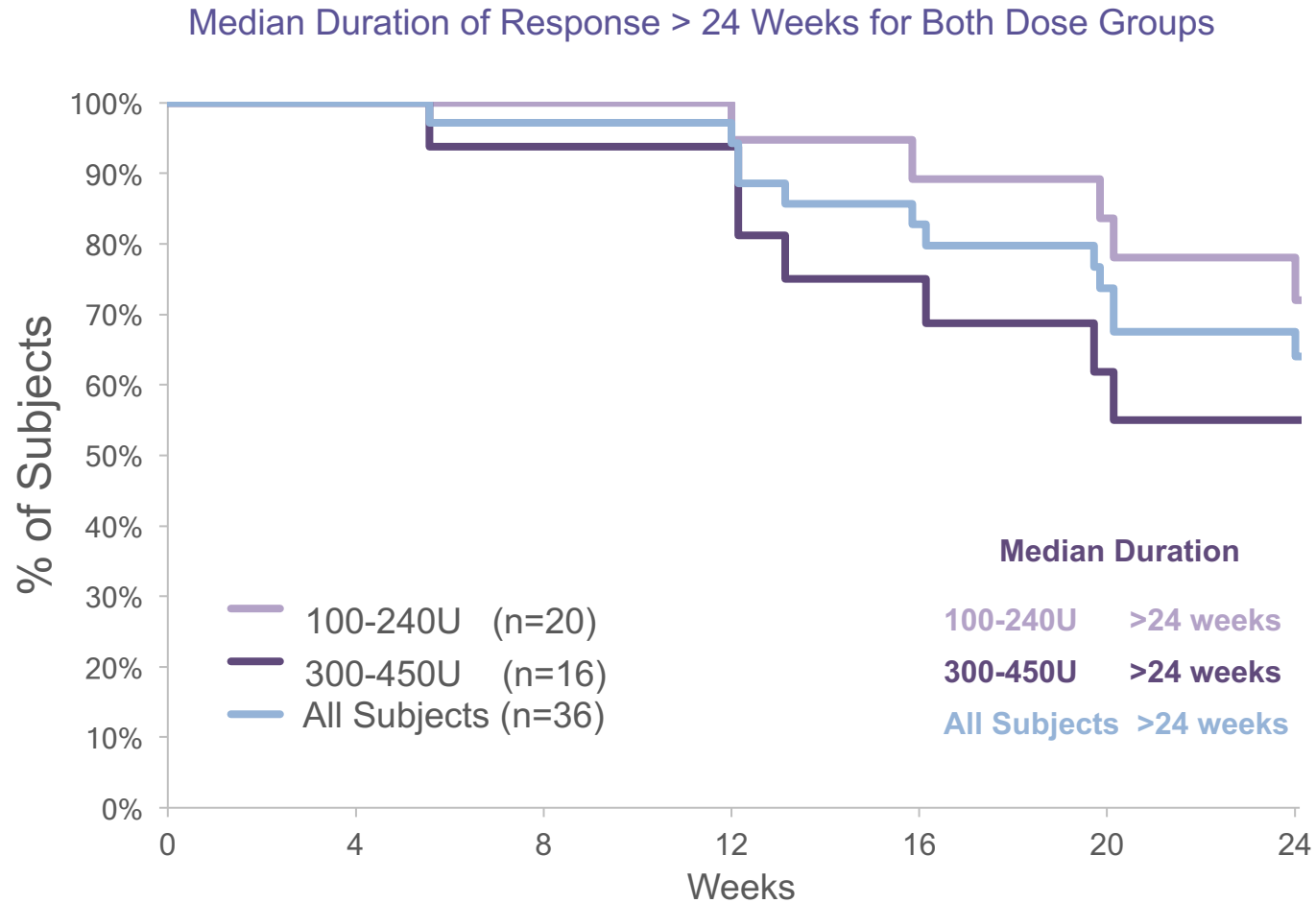
## By Dose Group

Clinically meaningful reduction in TWSTRS-Pain Score of 34% for all subjects beginning at Week 2, with the majority of this benefit maintained through Week 24 in both dose groups



# Duration of Effect

Defined by % Subjects Maintaining  $\geq 20\%$  of Treatment Benefit\*

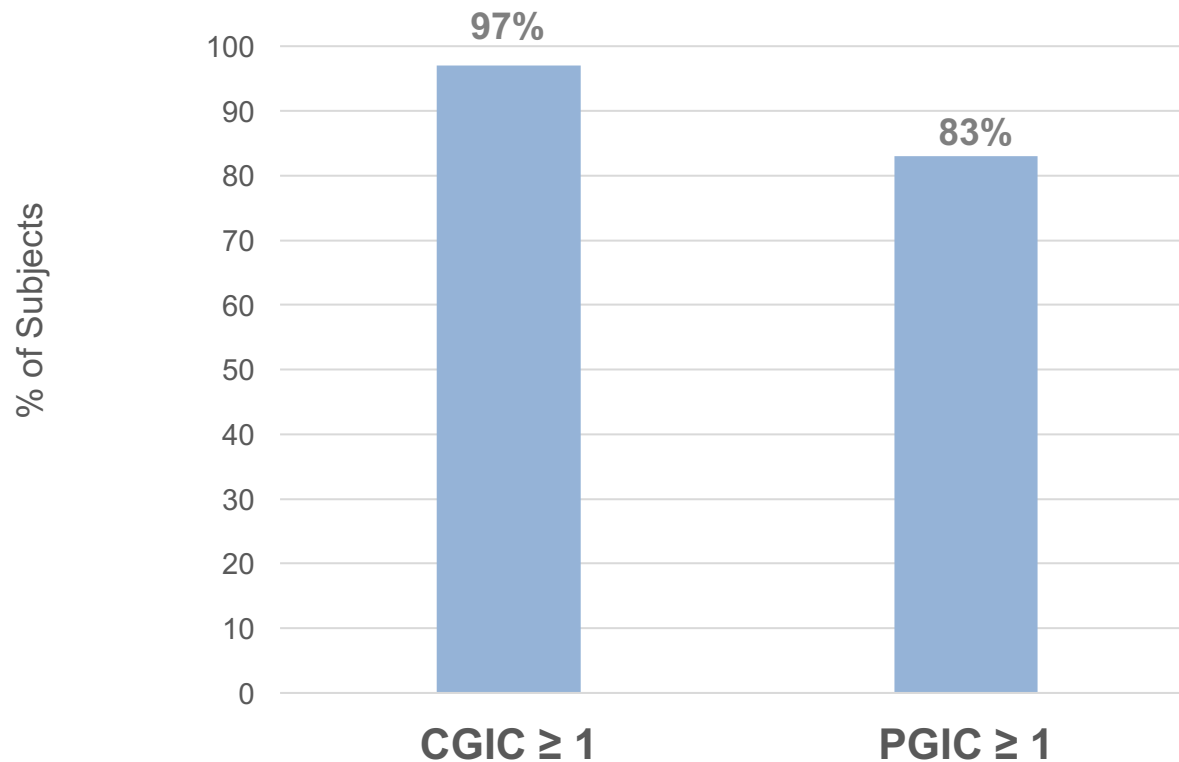


\*Of subjects with Improvement at Week 4. Withdrawals due to need for retreatment are considered as events. Treatment benefit defined as the reduction in TWSTRS-Total score at Week 4.

# Response Rate by Global Impression of Change at Week 4

## All Subjects (n=35\*)

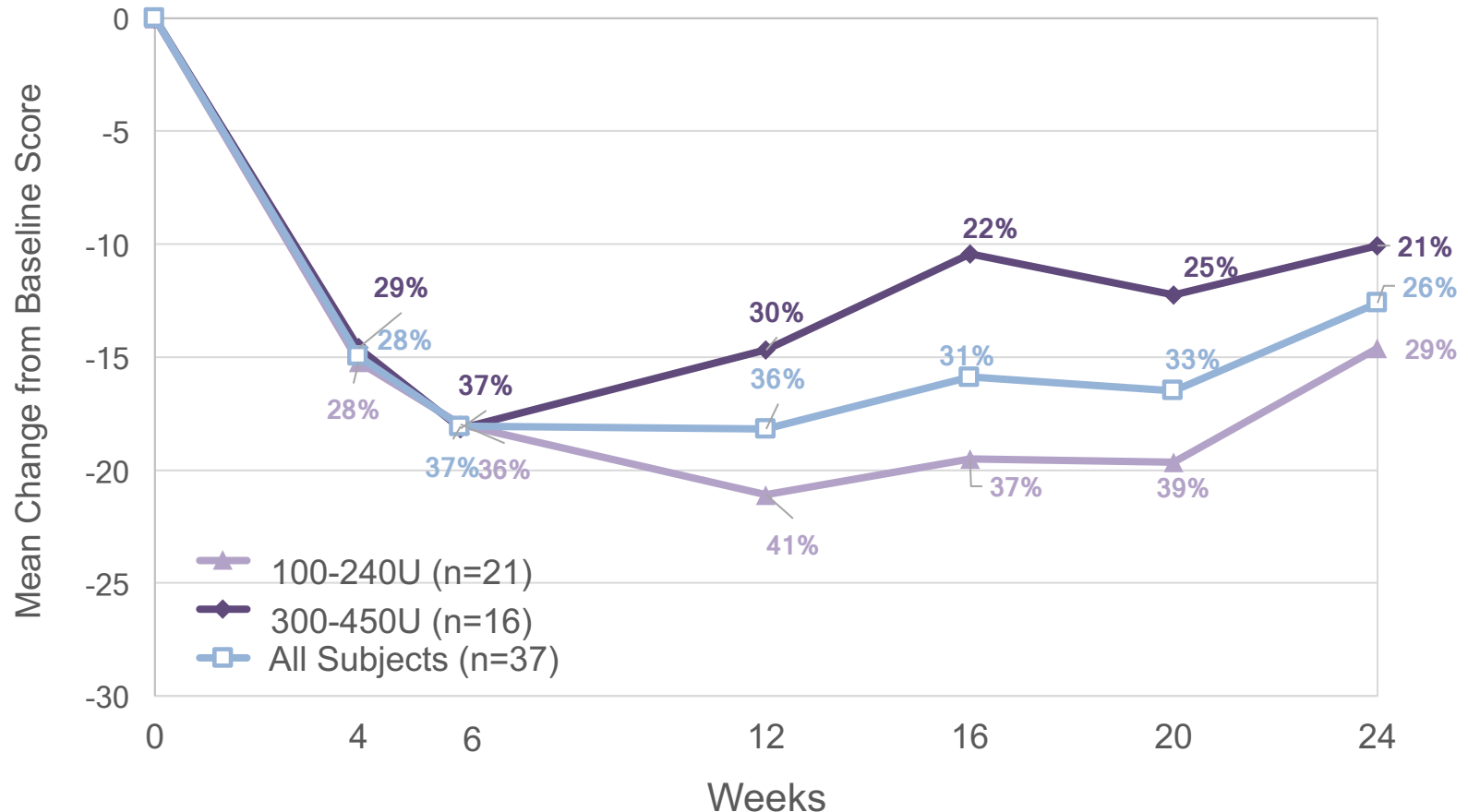
97% of all subjects on CGIC<sup>†</sup> and 83% of all subjects on PGIC<sup>††</sup> experienced an improvement in CD signs and symptoms (Score  $\geq 1$ ) at Week 4



\*Two subjects missed Week 4 visit. <sup>†</sup>Clinician Global Impression of Change; <sup>††</sup>Patient Global Impression of Change

# Quality of Life: Reduction in CDIP-58\* Score Over Time By Dose Group

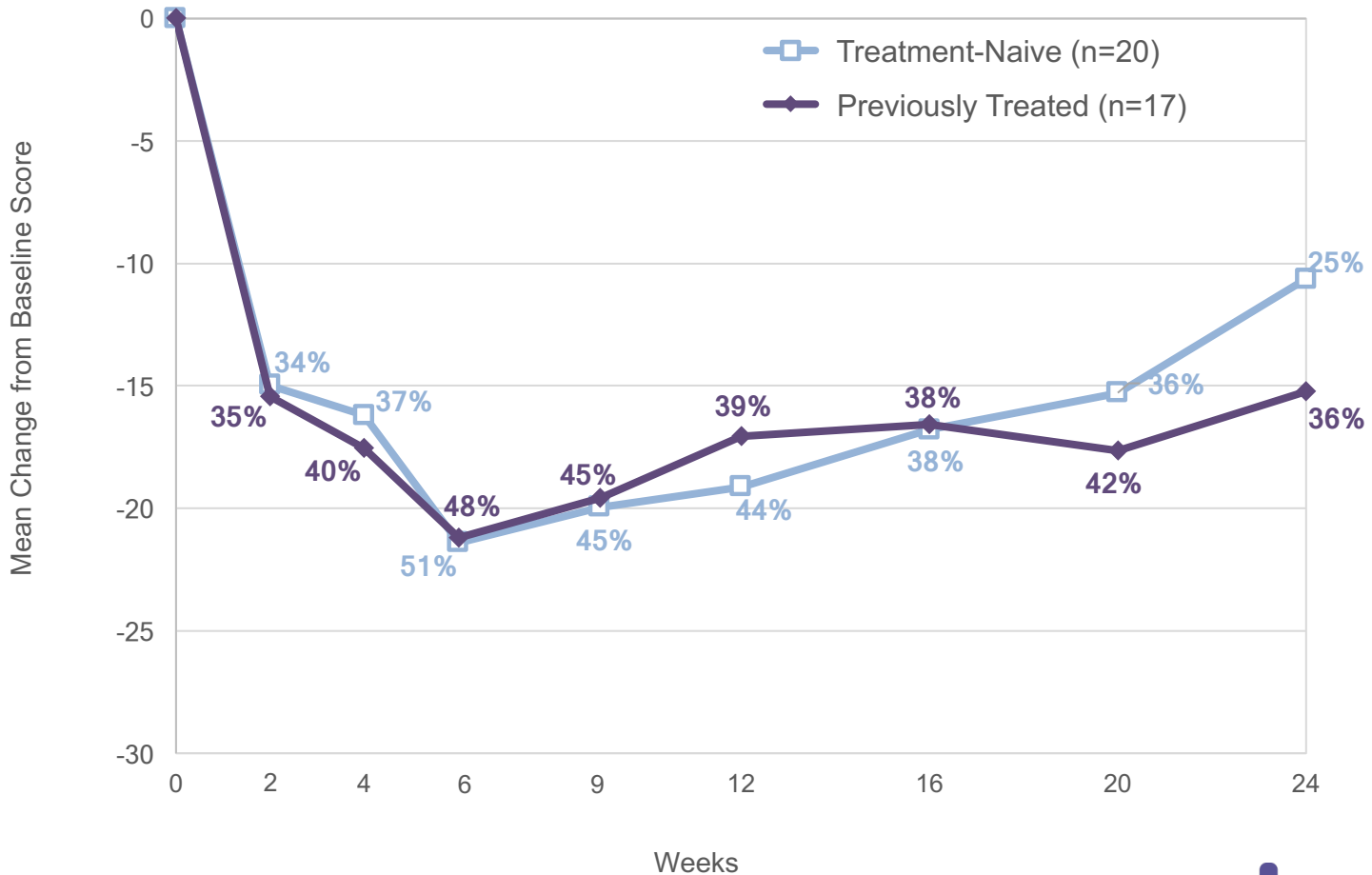
Clinically meaningful reduction of 37% in CDIP-58 Score observed at Week 6 for all subjects, with the majority of this benefit maintained through Week 24



\* Cervical Dystonia Impact Profile-58 Quality of Life Measure

# Reduction in TWSTRS-Total Score Over Time By Prior BoNT Treatment

A clinically meaningful reduction in TWSTRS-Total Score of 37-41% was observed at Week 4, with the majority of this benefit maintained through Week 24 regardless of prior BoNT treatment



# Efficacy Summary

- **Duration of Effect of > 24 Weeks:** Median duration of effect, defined as subjects maintaining  $\geq 20\%$  of the Week 4 treatment benefit (Target TWSTRS Score), was > 24 Weeks for both dose groups (Group A: 100-240U and Group B: 300-450U).
- **Improvement in Cervical Dystonia Signs and Symptoms:** A clinically significant mean reduction from baseline in the TWSTRS-Total Score of 16.8 (or 38%) was observed at Week 4 across all subjects.
  - Therapeutic benefit peaked at Week 6 with 50% mean reduction from baseline, and was maintained at  $\geq 30\%$  through Week 24.
  - Clinically meaningful reductions in TWSTRS-Severity, -Disability and -Pain Subscales were consistent and also observed at all time points.
- **Quality of Life:** Meaningful reduction in CDIP-58 score of 37% (mean reduction of 18.1) was observed at Week 6, the majority of which was maintained (26%, mean reduction of 12.6) through Week 24 across all subjects.
- A clinically meaningful improvement in TWSTRS-Total Score of  $\geq 37\%$  was observed at Week 4 regardless of whether subjects had previously received BoNT treatment.

# Safety Summary

- RT002 appeared to be safe and generally well tolerated in both dose groups through Week 24, with no increase in treatment-emergent adverse events (TEAEs) upon dose escalation. All except one TEAE were mild or moderate in severity and no serious AEs were reported.
- Total of 22 treatment-related AEs in 13 of 37 subjects (35%) were reported and all resolved.
  - Reported in  $\geq 2$  cases included: dysphagia (14%), injection site erythema (8%), injection site bruising (5%), injection site pain (5%), muscle tightness (5%), and muscle weakness (5%).
- Treatment-related AEs of special interest had similar or lower incidence rates vs. prior BoNT-A studies.
  - Dysphagia: 14% (5/37; all mild); average duration 35 days.
  - Muscular weakness: 5% (2/37, 1 mild, 1 moderate), both local.
  - Neck pain: 3% (1/37; only severe TEAE reported), duration of 2 days.