

MariTide Update

June 23, 2025

AMGEN



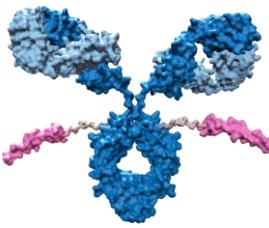
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The scientific information discussed in this presentation related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Further, any scientific information discussed in this presentation relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the products. The products are not approved for the investigational use(s) discussed in this presentation, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

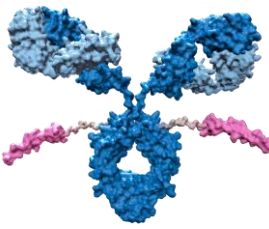


MariTide: A Unique, Differentiated and Competitive Profile

- First obesity treatment with monthly or less frequent dosing
- Strong efficacy with up to ~20% weight loss without a plateau at 52 weeks
- Meaningful improvements in cardiometabolic parameters including HbA1c, systolic blood pressure, and high-sensitivity C-reactive protein
- Tolerability consistent with the GLP-1 class for gastrointestinal adverse events and overall
- Dose escalation significantly improves tolerability without compromising weight loss efficacy
- Phase 3 MARITIME chronic weight management studies underway with further optimized three-step dose escalation for additional tolerability improvements
- MariTide's simple and convenient dosing can potentially improve adherence and long-term weight control, providing the opportunity to optimize health outcomes for people living with obesity and obesity related conditions including Type 2 diabetes

MariTide Update

Today's Topics



1

52-Week Data from Part 1 of the Phase 2 study

2

Phase 1 Pharmacokinetic Low Dose Initiation Study

3

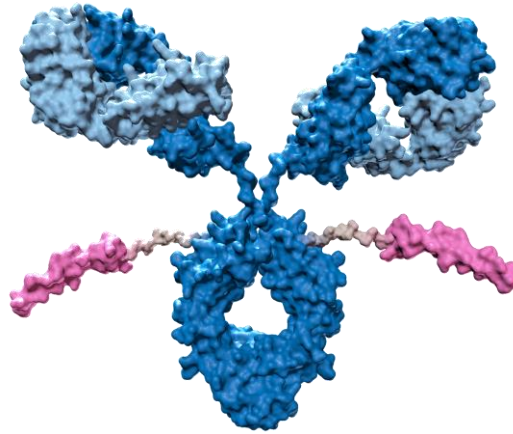
Phase 3 Chronic Weight Management Study Design

4

MariTide Data Generation

MariTide: First Monthly or Less Frequent Treatment for Obesity and Type 2 Diabetes

Monoclonal (anti-GIPR) antibody backbone with long half-life enables monthly or less frequent dosing



Two GLP-1R analog peptides positioned for optimal efficacy

MariTide's simple and convenient dosing can potentially improve adherence and long-term weight control, providing the opportunity to optimize health outcomes for people living with obesity

GIPR = glucose-dependent insulintropic polypeptide receptor; GLP-1R = glucagon-like peptide 1 receptor.
Véniant MM, Lu SC, Atangan L, et al. *Nat Metab.* 2024;6(2):290-303.

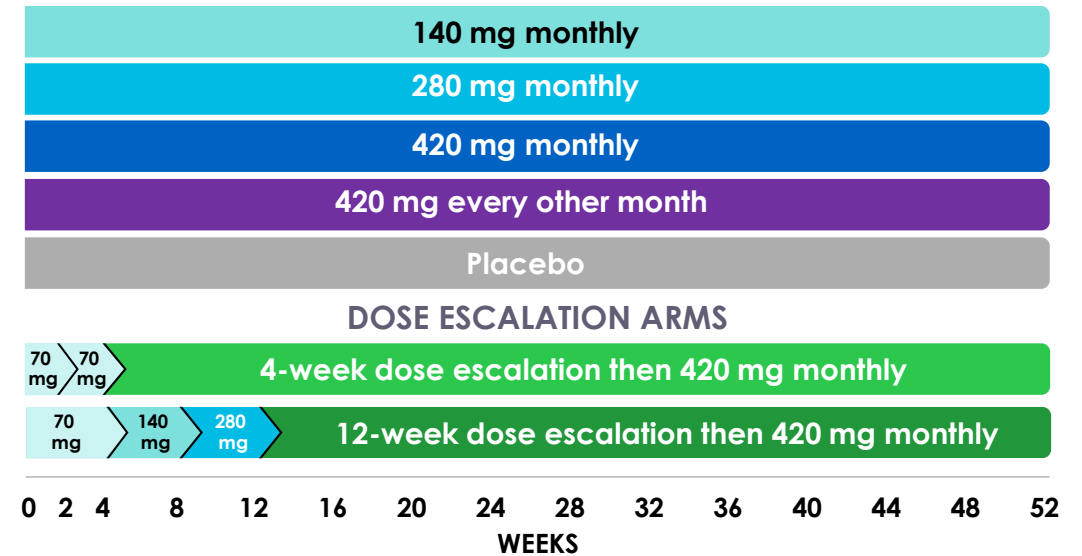
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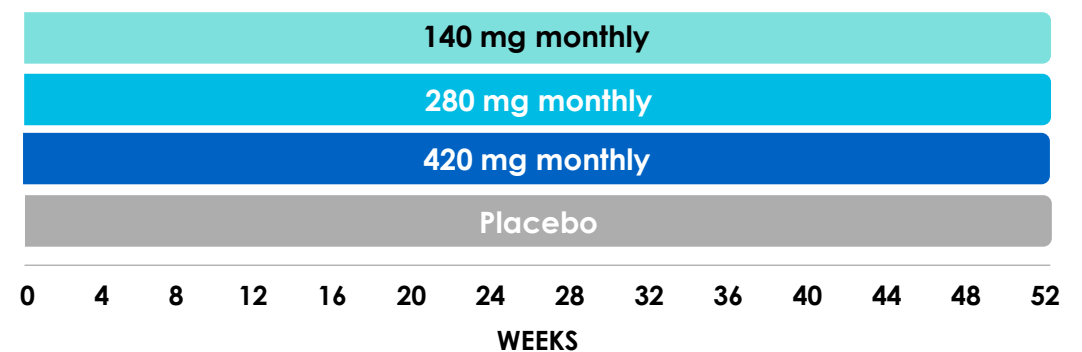
Overview of MariTide Phase 2 Study (Part 1)

- **52 week duration**
- **2 cohorts**
 1. Adults living with obesity or overweight WITHOUT Type 2 diabetes
 2. Adults living with obesity or overweight WITH Type 2 diabetes
- **592 adult patients**
- **11 arms, including 2 rapid dose escalation arms which both initiated with a 70 mg dose**
- **Monthly or less frequent dose schedules**

Obesity or Overweight WITHOUT Type 2 Diabetes (n=465)



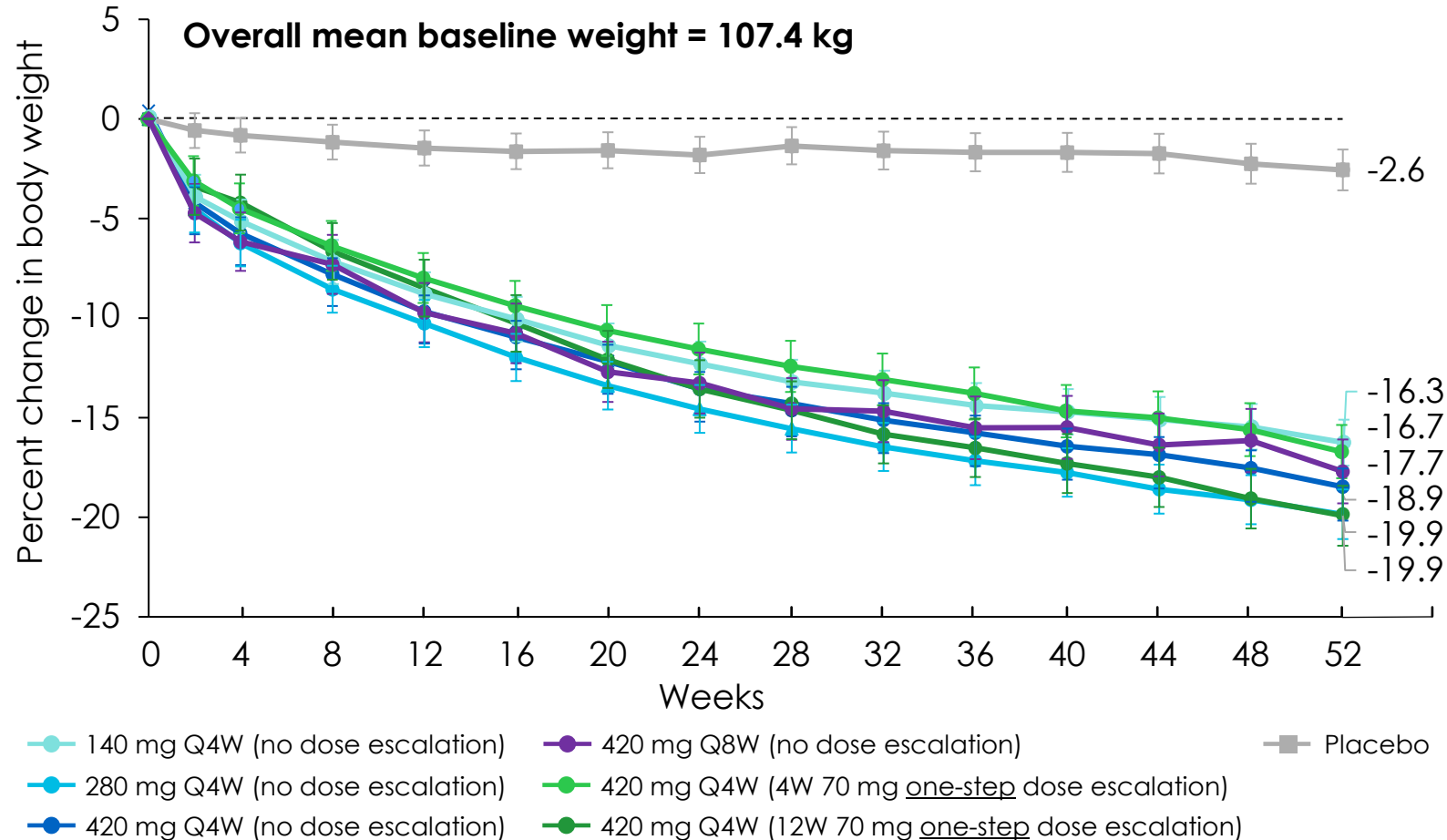
OBESITY or Overweight WITH Type 2 Diabetes (n=127)



mg = milligram.

MariTide Demonstrated Consistent Weight Loss Across All Target Dose Arms in Adults With Obesity WITHOUT Type 2 Diabetes

OBSESITY OR OVERWEIGHT
WITHOUT
TYPE 2 DIABETES



- MariTide demonstrated up to ~20% average weight loss without a plateau at 52 weeks
- Confirmed efficacy of monthly dosing with potential for less frequent dosing
- No weight loss plateau in any arm at 52 weeks
- Up to ~98% of patients lost ≥5% of their body weight

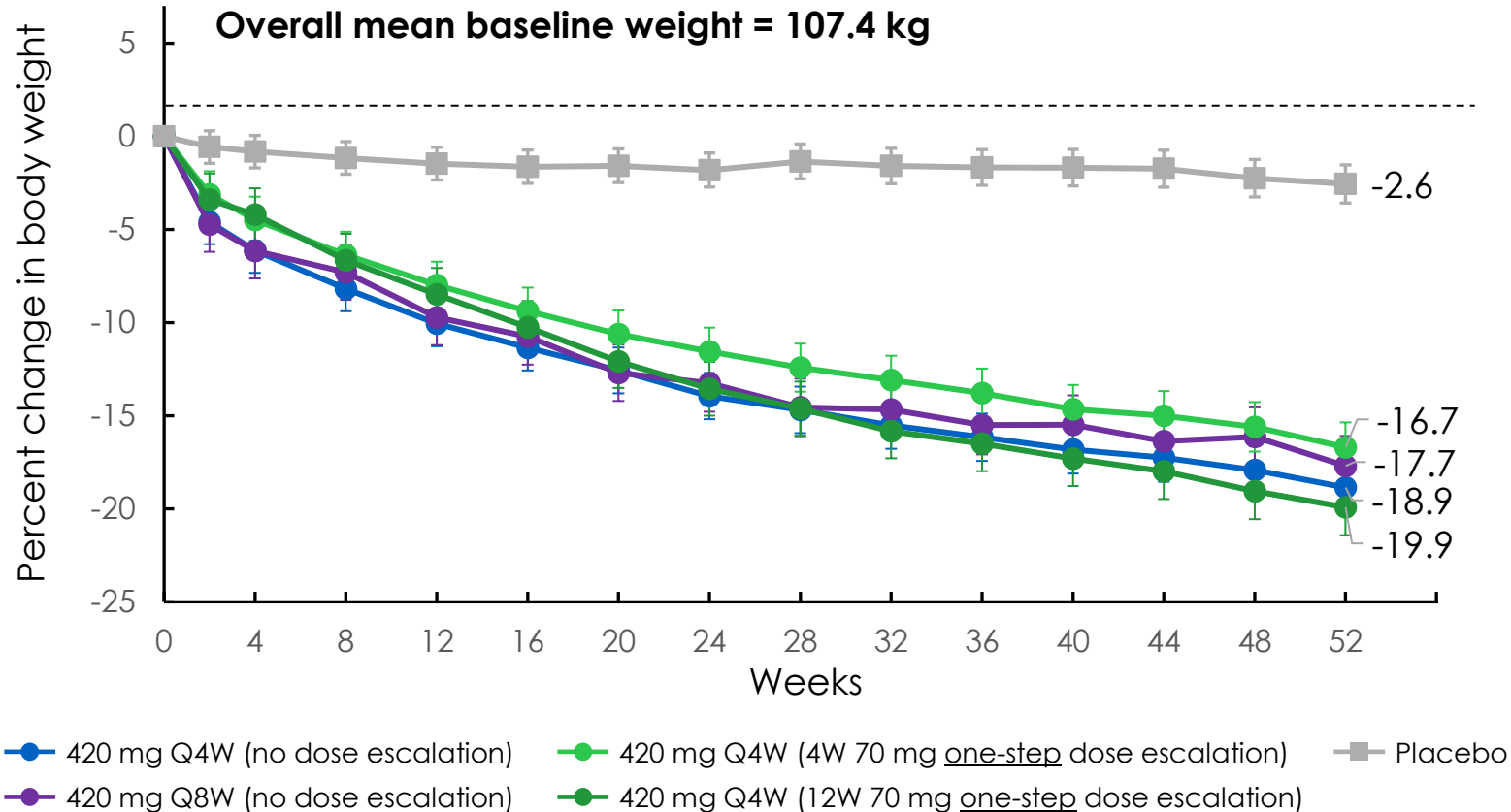
Substantial and statistically significant weight loss in all treatment arms

These and all subsequent efficacy data reported are based on a standard analytical measure commonly used for obesity medicines, the efficacy estimand. kg = kilograms; mg = milligrams; Q4W = every 4 weeks; Q8W = every eight weeks.



Dose Escalation and Every Other Month Dosing of MariTide Demonstrated Efficacy Comparable to 420 mg Monthly Dosing

OBSESITY OR OVERWEIGHT
WITHOUT
TYPE 2 DIABETES



- Dose escalation resulted in similar magnitude of weight loss compared to no dose escalation
- Every other month dosing resulted in significant weight loss, reinforcing potential for less frequent dosing

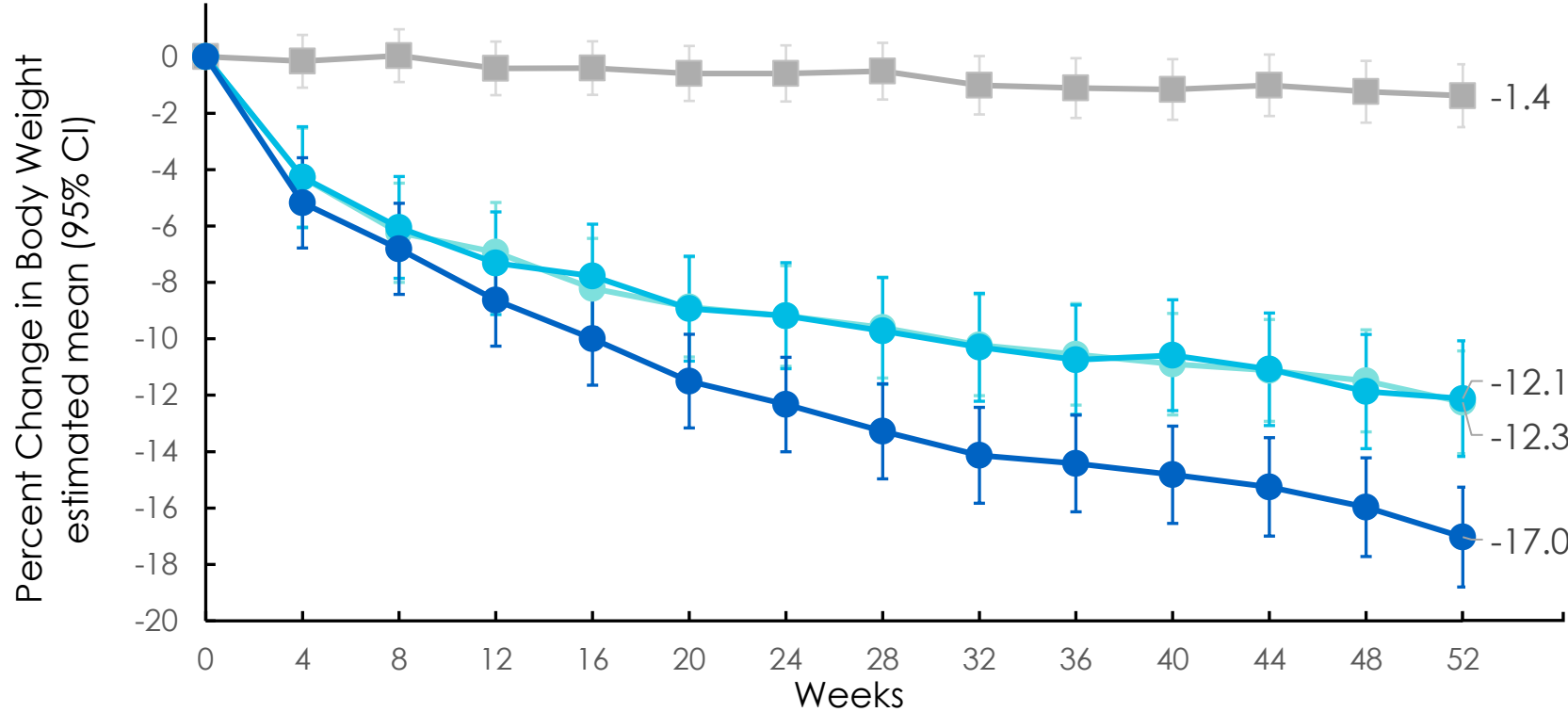
Substantial and statistically significant weight loss in all treatment arms

These and all subsequent efficacy data reported are based on a standard analytical measure commonly used for obesity medicines, the efficacy estimand. kg = kilogram; mg = milligram; Q4W = every 4 weeks; Q8W = every eight weeks.



MariTide Demonstrated an Impressive Up to ~17% Average Weight Loss at 52 Weeks Without a Weight Loss Plateau in Adults With Obesity WITH Type 2 Diabetes

OBEESITY OR OVERWEIGHT
WITH
TYPE 2 DIABETES



- Substantial and statistically significant weight loss in all treatment arms
- Confirmed efficacy of monthly dosing
- No weight loss plateau in any arm, indicating the potential for further weight loss beyond 52 weeks
- Up to ~99% of patients lost ≥ 5% of their body weight

● 140 mg Q4W (no dose escalation) ● 420 mg Q4W (no dose escalation)

● 280 mg Q4W (no dose escalation) ■ Placebo

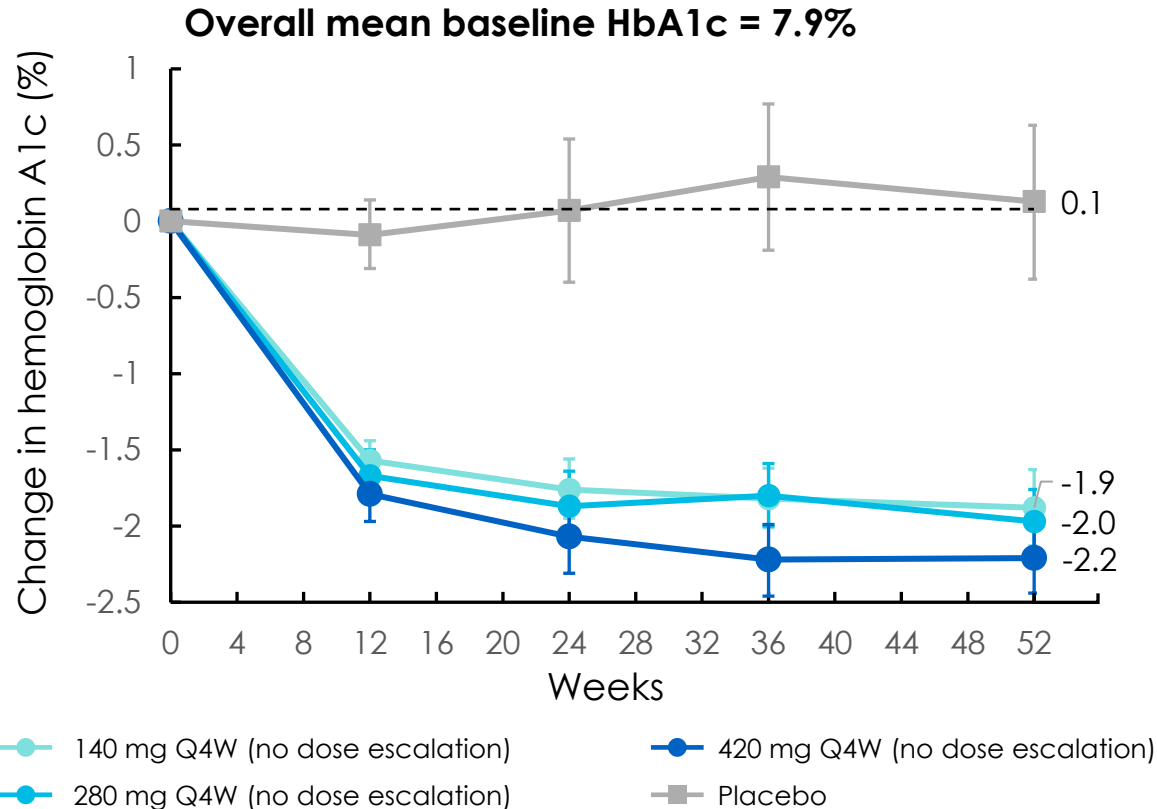
These and all subsequent efficacy data reported are based on a standard analytical measure commonly used for obesity medicines, the efficacy estimand. mg = milligrams; Q4W = every 4 weeks; CI = confidence interval.

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MariTide Demonstrated Significant and Clinically Meaningful Improvements in Cardiometabolic Parameters in Adults With Obesity WITH Type 2 Diabetes

OBSESITY OR OVERWEIGHT
WITH
TYPE 2 DIABETES



SELECT CARDIOMETABOLIC RISK FACTORS	CHANGE FROM BASELINE TO W52 FOR PLACEBO	CHANGE FROM BASELINE TO W52 FOR MARITIDE 420 mg MONTHLY
HbA1c	+0.1%	- 2.2%*
Glucose	+22 mg/dL	- 58 mg/dL*
Systolic blood pressure	-2 mmHg	- 11 mmHg*
Triglycerides	+21%*	- 28%*
hs-CRP	-25%	- 72%*

*statistically significant from baseline.

These and all subsequent efficacy data reported are based on a standard analytical measure commonly used for obesity medicines, the efficacy estimand. LDL-C was similar between placebo and MariTide 420 mg.

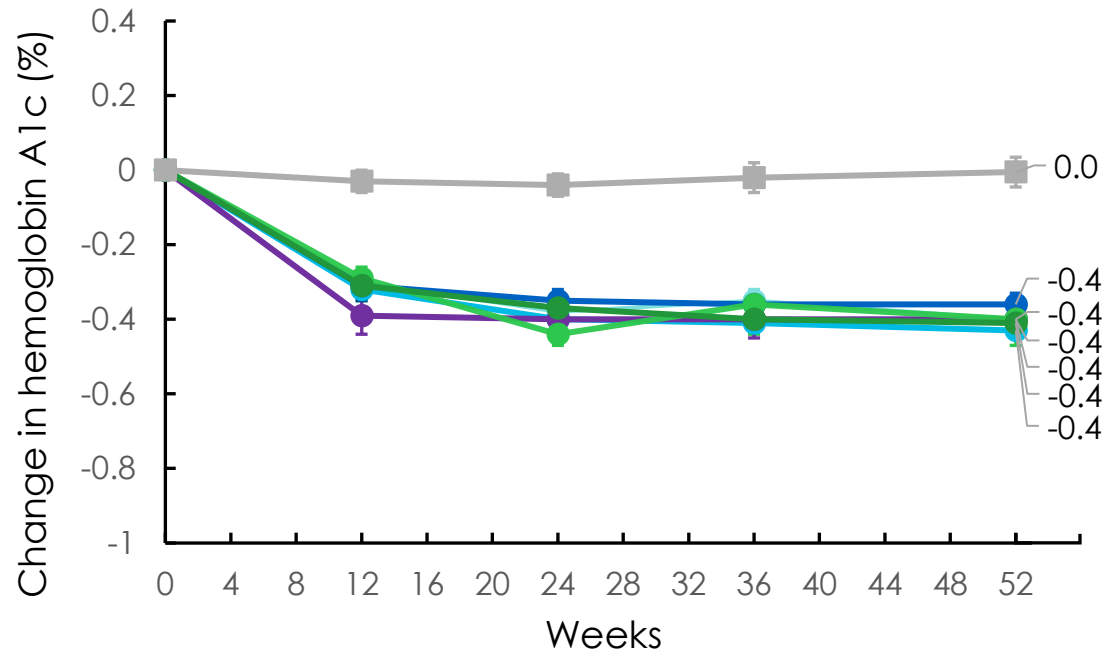
dl = deciliter; HbA1c = hemoglobin A1c; hsCRP = high-sensitivity C-reactive protein; LDL-C = low-density lipoprotein cholesterol; mg = milligrams; mmHg = millimeters of mercury; Q4W = every 4 weeks; W52 = week 52.



MariTide Demonstrated Significant and Clinically Meaningful Improvements in Cardiometabolic Parameters in Adults With Obesity WITHOUT Type 2 Diabetes

OBESITY OR OVERWEIGHT
WITHOUT
TYPE 2 DIABETES

Overall mean baseline HbA1c = 5.5%



- 140 mg Q4W (no dose escalation)
- 280 mg Q4W (no dose escalation)
- 420 mg Q4W (no dose escalation)
- 420 mg Q4W (12W 70 mg one-step dose escalation)
- 420 mg Q4W (4W 70 mg one-step dose escalation)
- 420 mg Q8W (no dose escalation)
- Placebo

SELECT CARDIOMETABOLIC RISK FACTORS	CHANGE FROM BASELINE TO W52 FOR PLACEBO	CHANGE FROM BASELINE TO W52 FOR POOLED 420 MARITIDE DOSE ARMS
Systolic blood pressure	- 3 mmHg	- 11 mmHg*
LDL-C	+1%	- 5%*
Triglycerides	+1%	- 19%*
hs-CRP	+1%	- 53%*

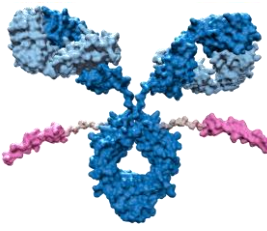
Across all arms, between 70% and 96% of patients with prediabetes (HbA1c 5.7-6.4%) at baseline achieved an HbA1c <5.7%

*statistically significant from baseline.

These and all subsequent efficacy data reported are based on a standard analytical measure commonly used for obesity medicines, the efficacy estimand.

HbA1c = hemoglobin A1c; hs-CRP = high-sensitivity C-reactive protein; LDL-C = low-density lipoprotein cholesterol; mmHg = millimeters of mercury; Q4W = every 4 weeks; Q8W = every 8 weeks; W52 = week 52.



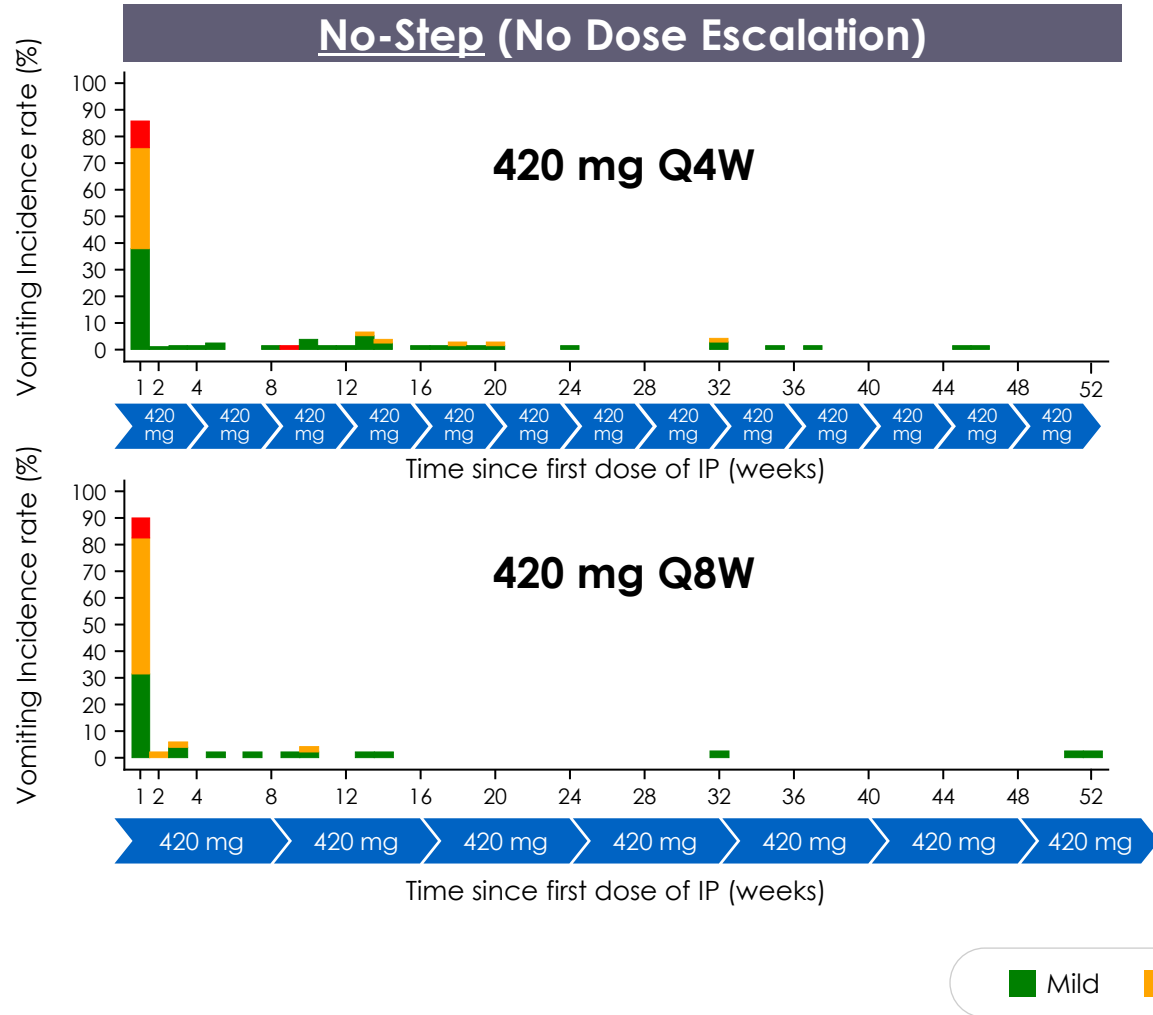


Findings From Multiple Studies Provide the Insights to Optimize MariTide's Tolerability Profile in Phase 3

- Overall safety consistent with GLP-1 class
- Efficacy is durable, while gastrointestinal adverse events are short lived and predominantly associated with initial doses of MariTide
- MariTide is well tolerated at target dose
- Dose escalation significantly improves tolerability during initial dosing
 - With one-step dose escalation in the Phase 2 study, vomiting incidence was reduced and discontinuation rate due to GI AEs was low (8%)
 - Two-step dose escalation in the Phase 1 Low Dose Initiation study further reduced vomiting incidence with no discontinuation due to GI AEs

In Part 1 of the Phase 2 Study, MariTide was Well Tolerated at Target Doses

OBSESITY OR OVERWEIGHT
WITHOUT
TYPE 2 DIABETES

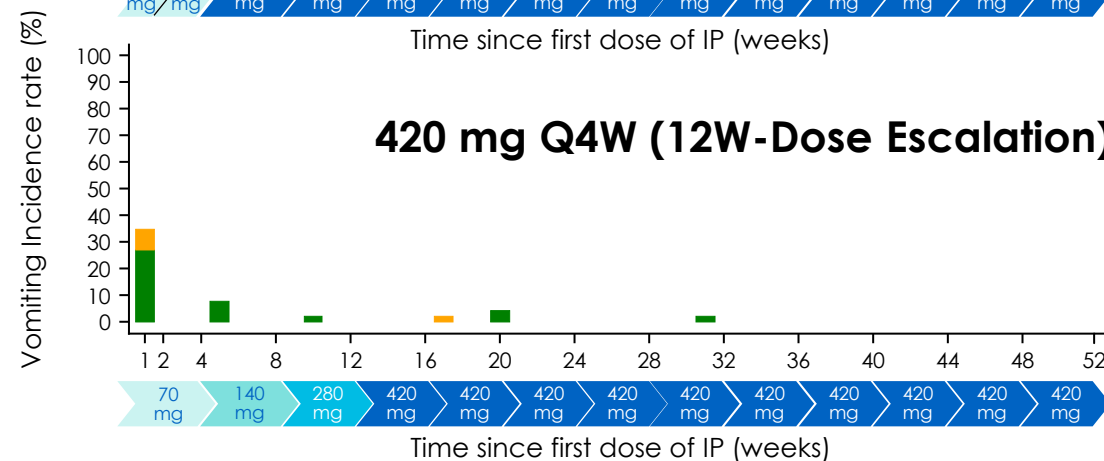
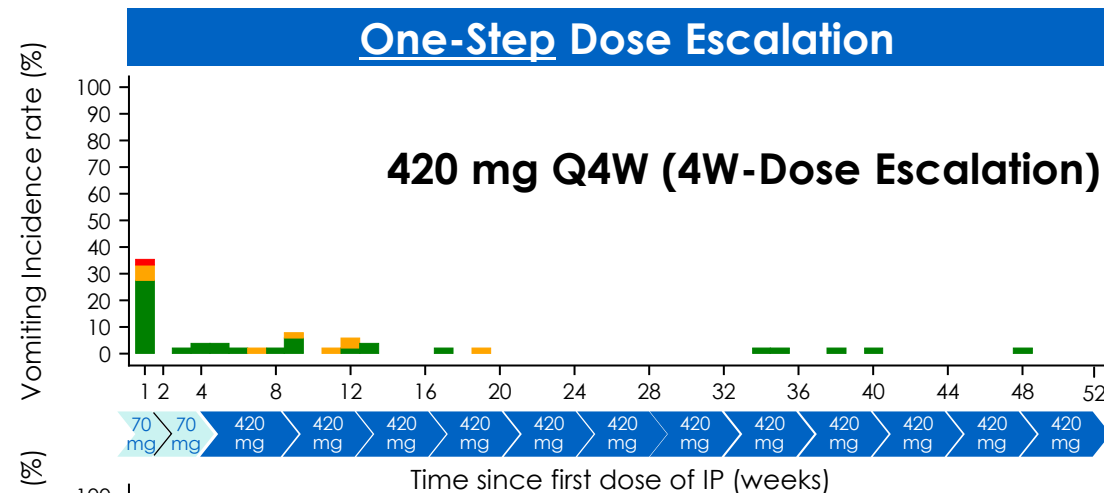
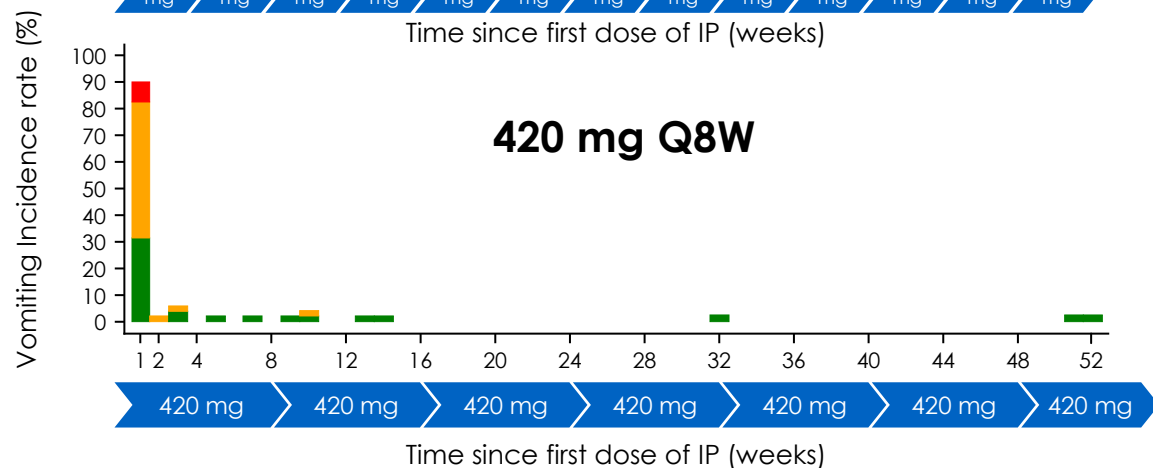
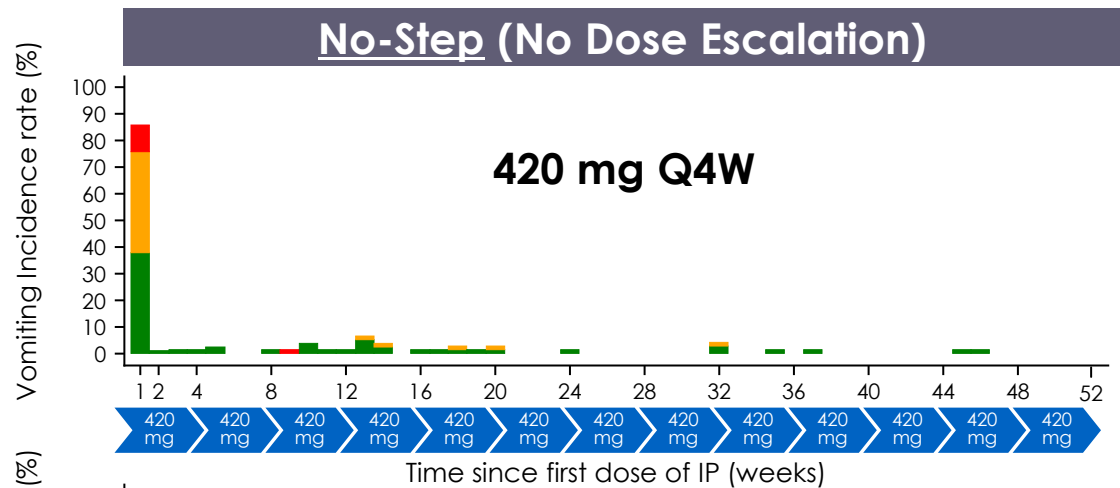


The incidence graph captures the proportion of subjects who have an AE start within the period captured. For example, during week 1, this is the proportion of subjects with a new AE reported during days 1-7.

IP = investigational product; mg = milligrams; Q4W = every 4 weeks; Q8W = every 8 weeks; AE = adverse event.

MariTide Tolerability was Improved at Initiation With One-Step Dose Escalation

OBSESITY OR OVERWEIGHT
WITHOUT
TYPE 2 DIABETES



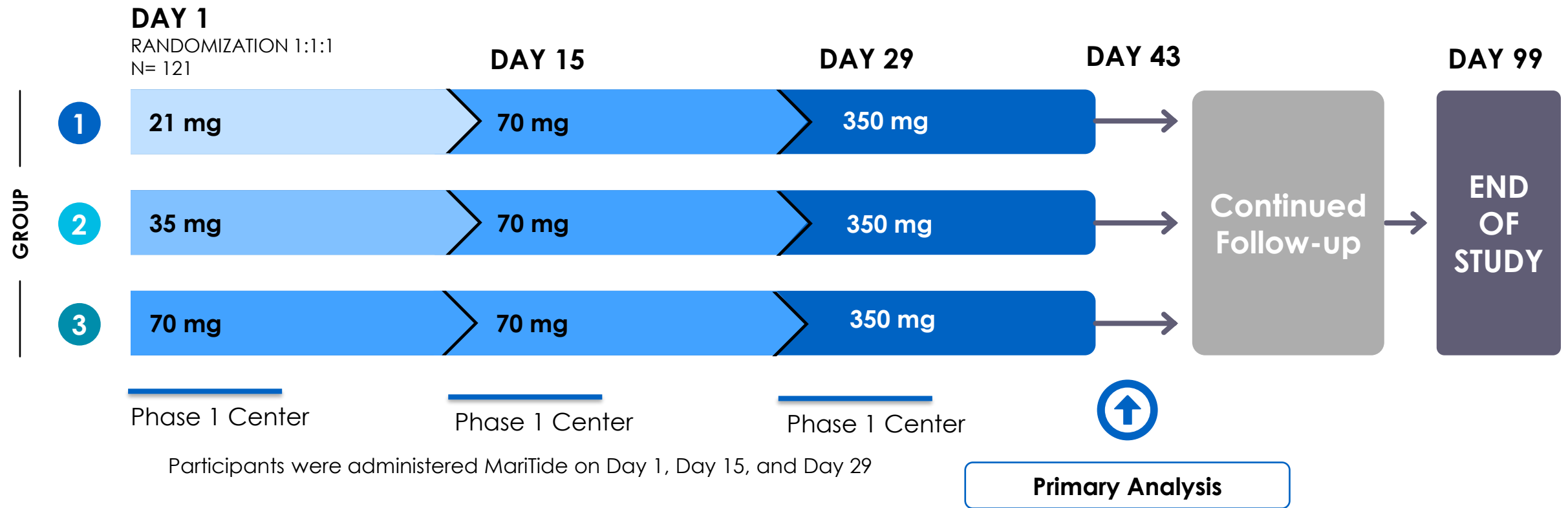
■ Mild ■ Moderate ■ Severe

The incidence graph captures the proportion of subjects who have an AE start within the period captured. For example, during week 1, this is the proportion of subjects with a new AE reported during days 1-7.

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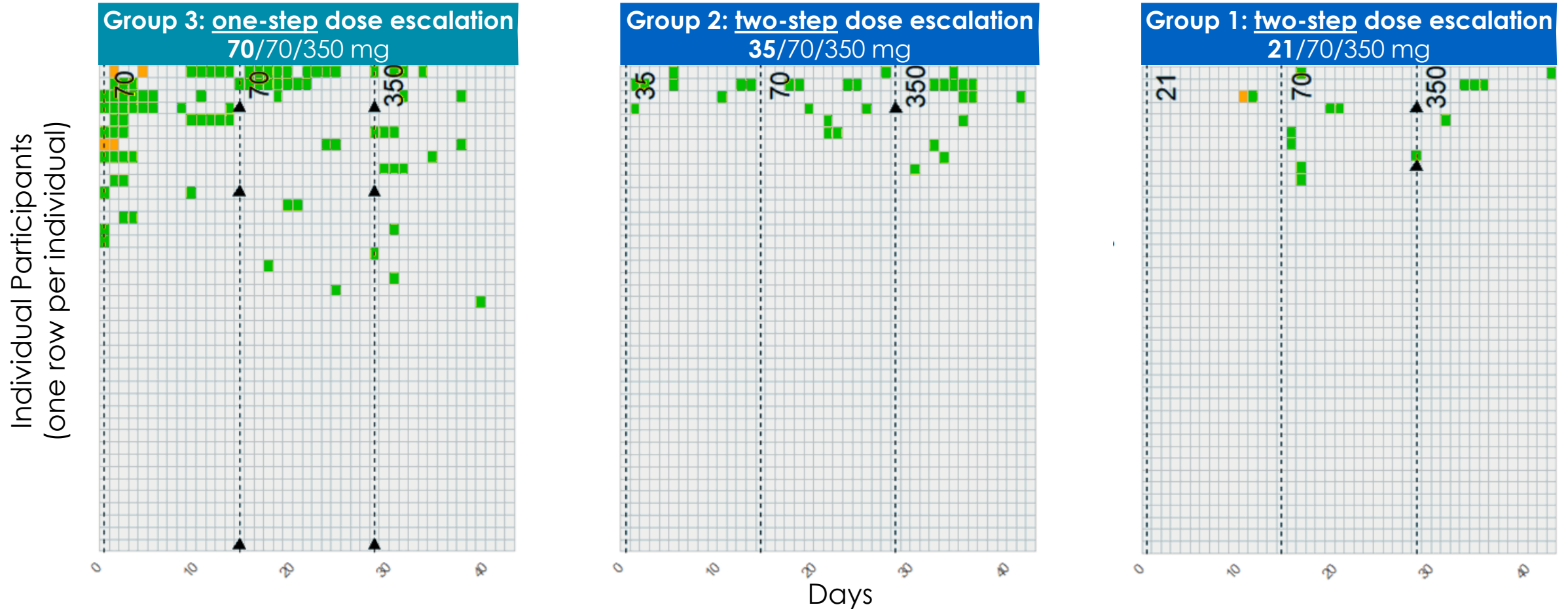
Two-Step Dose Escalation was Evaluated Through a Phase 1 Low Dose Initiation Study



A Randomized, Double-Blind, Multiple-Dose Study.
Double-blind administration using placebo double-dummy.
mg = milligrams.

Two-Step Dose Escalation Improved Incident GI Adverse Events and Reinforced That Events Were Short Lived

No event
 Mild
 Moderate
 Severe
 ▲ Missed Dose



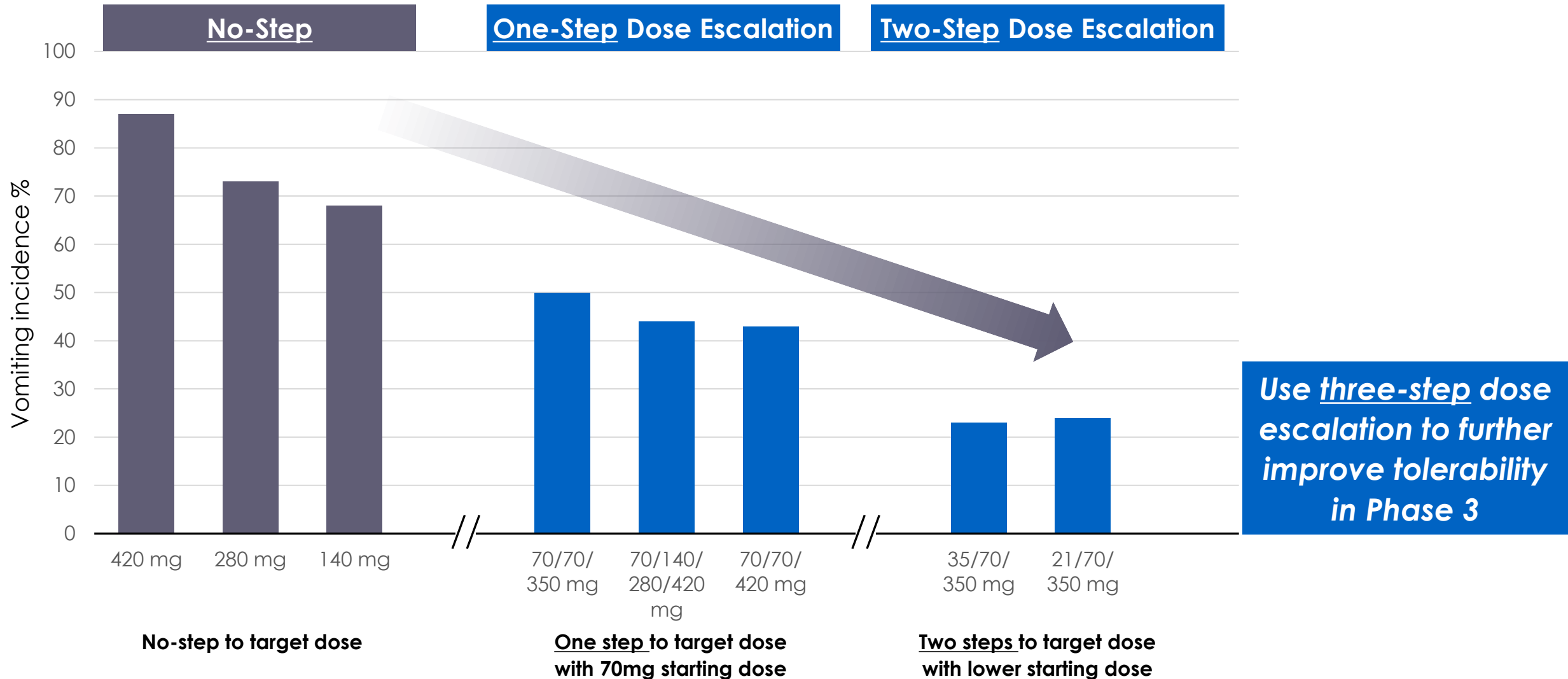
GI adverse events are short lived and predominantly clustered with the initial doses of MariTide

Participants were administered MariTide on Day 1, Day 15, and Day 29.

GI = gastrointestinal; mg = milligrams.



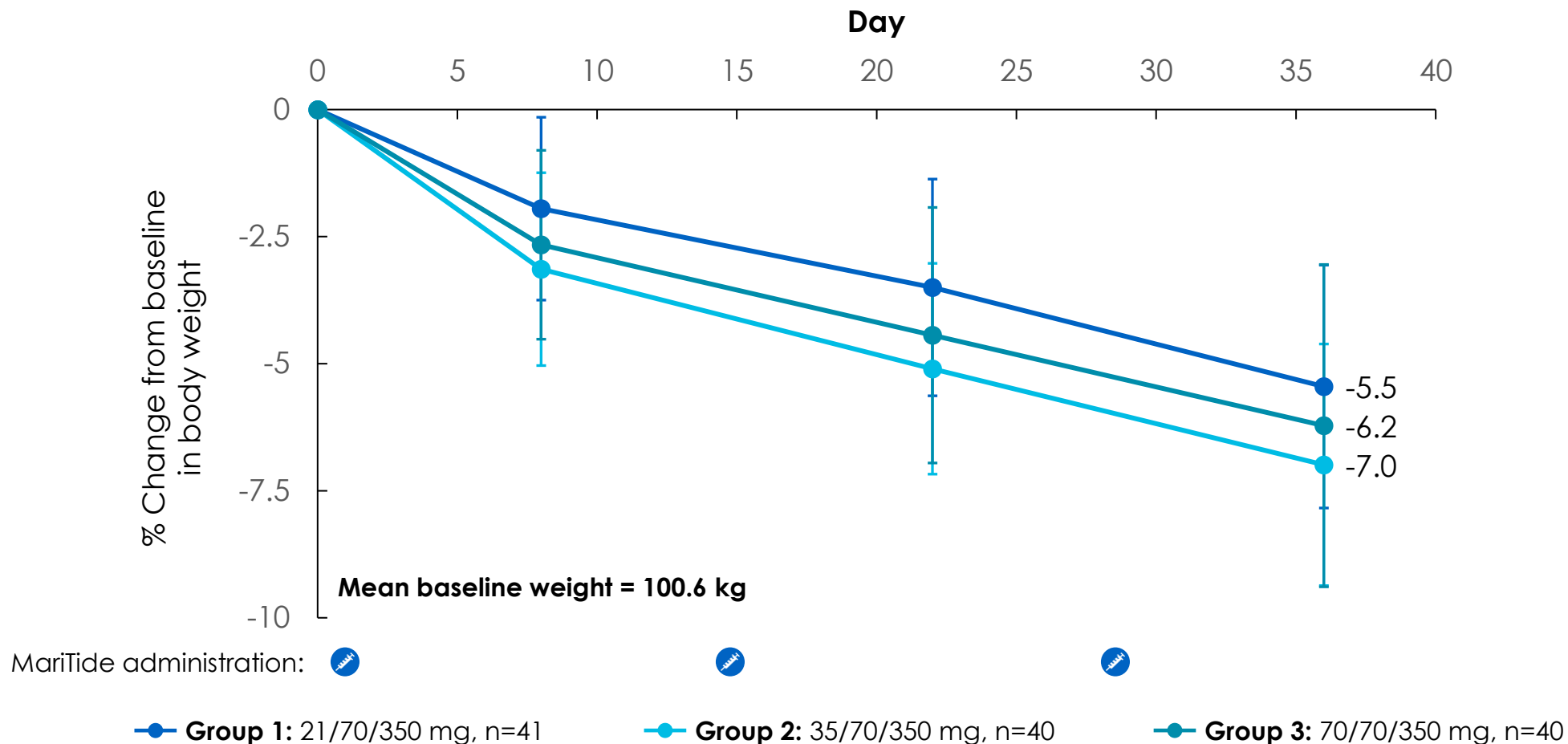
Meaningful Improvements in Tolerability Observed With Each Additional Dose Escalation Step



mg = milligrams.



Dose Escalation in the MariTide Phase 1 Low Dose Initiation Study Delivered Meaningful Weight Loss



Participants were administered MariTide on Day 1, Day 15, and Day 29.

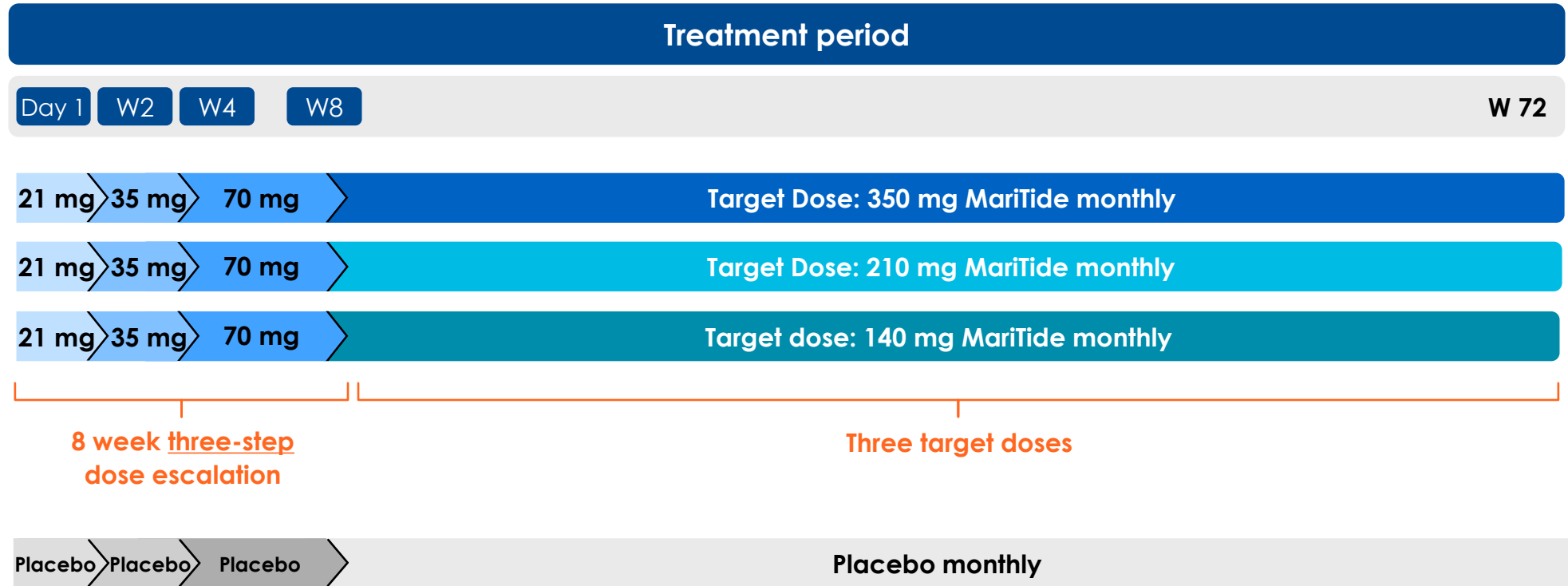
kg = kilograms; mg = milligrams.

Three-Step Dose Escalation Will be Used to Further Improve MariTide's Tolerability Profile in Phase 3

Dose Escalation	<u>No-Step</u>	<u>One-Step</u>	<u>Two-Step</u>	<u>Three-Step</u>
Study	Phase 2	Phase 2	Phase 1 LDI	Phase 3
Duration	-	2-4 weeks	4 weeks	8 weeks
Nausea Vomiting	High	Lower	Even Lower	Expect Further Improvement in Phase 3
Dosing Scheme	No-step to target dose	70 mg → Target dose	35 mg → 70 mg → Target 21 mg → 70 mg → Target	21mg → 35 mg → 70mg → Target

LDI = Low Dose Initiation Study; mg = milligrams.

MariTide Phase 3 Chronic Weight Management Study Designs WITH and WITHOUT Type 2 Diabetes



- 72-week duration to enable further long-term efficacy and durability evaluation
- Three target doses to accommodate a range of participant needs
- Optimized three-step dose escalation informed by pharmacokinetic analysis and GI adverse event learnings

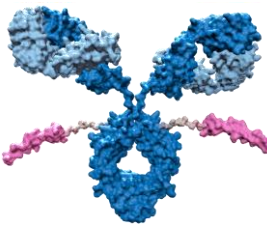
The 72-week treatment period includes a dose escalation period of 8 weeks and a 64-week target dose period.

Adjunct to reduced-calorie diet and increased physical activity.

Two studies, one in adult participants without Type 2 diabetes mellitus who have obesity or are overweight and the second in adult participants with Type 2 diabetes mellitus who have obesity or are overweight.

GI = gastrointestinal; mg = milligrams; W = week.

MariTide Data Generation



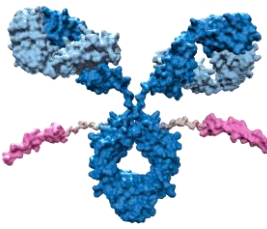
Additional Phase 3 study initiations

- Atherosclerotic Cardiovascular Disease Outcomes
- Heart failure
- Obstructive sleep apnea

Studies in Progress

- Phase 3 chronic weight management study in patients WITHOUT Type 2 diabetes
- Phase 3 chronic weight management study in patients WITH Type 2 diabetes
- Part 2 of the Phase 2 study
- Phase 2 Type 2 diabetes study

Key Takeaways

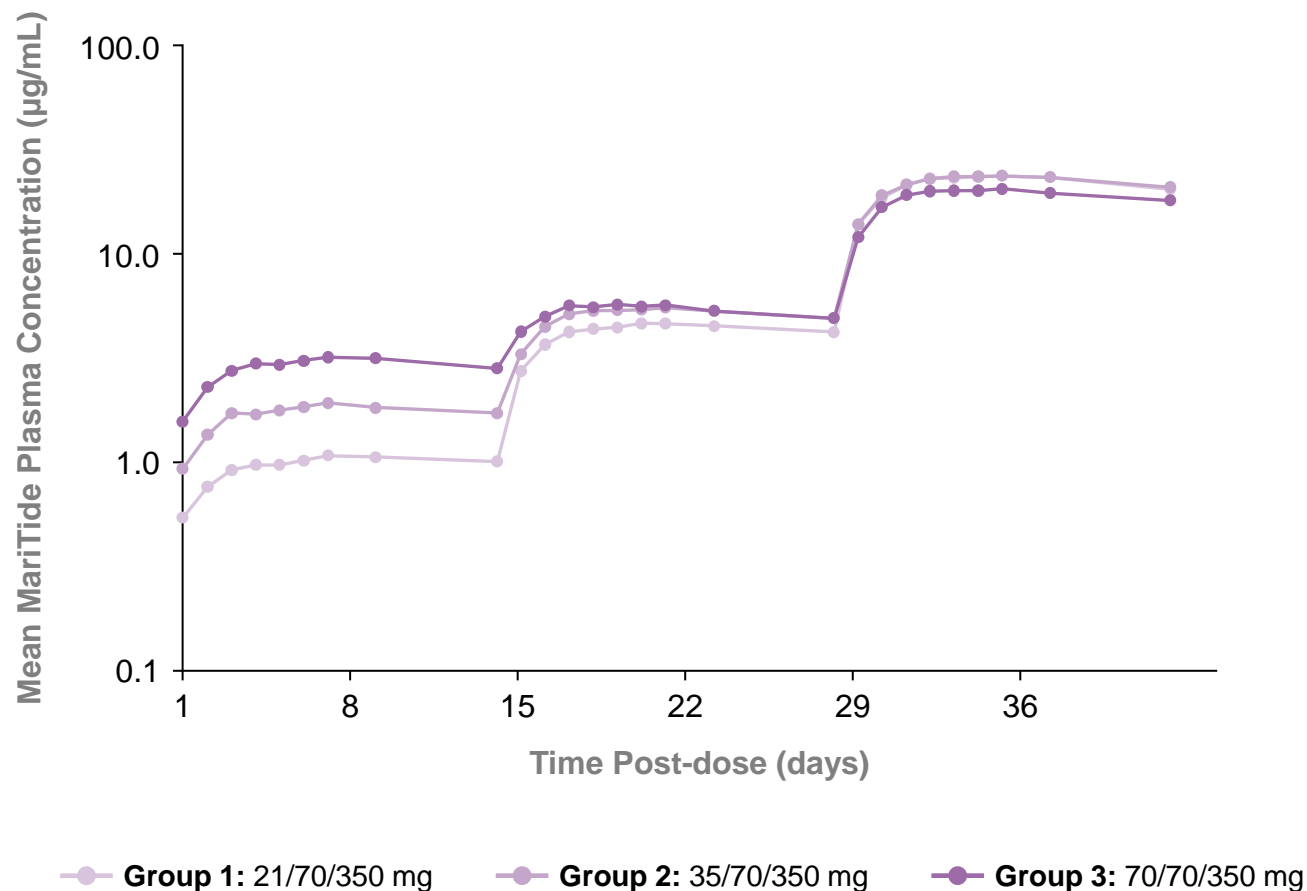


- **First obesity treatment with monthly or less frequent dosing**
- **Strong efficacy with up to ~20% weight loss without a plateau at 52 weeks**
- **Meaningful improvements in cardiometabolic parameters including HbA1c, systolic blood pressure, and high-sensitivity C-reactive protein**
- **Tolerability consistent with the GLP-1 class for gastrointestinal adverse events and overall**
- **Dose escalation significantly improves tolerability without compromising weight loss efficacy**
- **Phase 3 MARITIME chronic weight management studies underway with further optimized three-step dose escalation for additional tolerability improvements**
- **MariTide's simple and convenient dosing can potentially improve adherence and long-term weight control, providing the opportunity to optimize health outcomes for people living with obesity and obesity related conditions including Type 2 diabetes**

HbA1c = hemoglobin A1c; GLP-1 = glucagon-like peptide 1.

QUESTIONS?

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Day 1 (MariTide 21, 35, or 70 mg SC)

Group	t_{max} (day)	C_{max} (µg/mL)	AUC_{0-14} (day × µg/mL)
Group 1: 21/70/350 mg N = 41	9.0 (2.0-14.0)	1.08 (52.8%)	11.3 (59.0%)
Group 2: 35/70/350 mg N = 40	7.0 (3.0-14.1)	1.95 (47.9%)	20.6 (50.7%)
Group 3: 70/70/350 mg N = 40	7.0 (3.0-14.1)	3.24 (40.1%)	34.7 (41.4%)*

Day 15 (MariTide 70 mg SC)

Group	t_{max} (day)	C_{max} (µg/mL)	AUC_{0-14} (day × µg/mL)
Group 1: 21/70/350 mg N = 41	7.0 (2.0-14.1)	4.69 (46.5%)	54.0 (45.5%)†
Group 2: 35/70/350 mg N = 40	7.0 (3.0-14.1)	5.66 (38.9%)	64.9 (39.1%)
Group 3: 70/70/350 mg N = 40	5.0 (3.0-14.0)‡	5.82 (42.8%)‡	67.2 (41.3%)‡

Day 29 (MariTide 350 mg SC)

Group	t_{max} (day)	C_{max} (µg/mL)	AUC_{0-14} (day × µg/mL)
Group 1: 21/70/350 mg N=41	7.0 (3.0-14.0)*	23.2 (50.1%)*	267 (47.4%)*
Group 2: 35/70/350 mg N=40	7.0 (3.0-15.2)†	24.2 (32.2%)†	281 (32.5%)†
Group 3: 70/70/350 mg N=40	7.0 (2.0-9.1)‡	21.1 (38.1%)‡	237 (37.9%)‡

Data are presented as geometric mean (coefficient of variation, CV%), except for t_{max} , which is presented as median (range).†

MariTide plasma exposure generally increased with increasing Day 1 dose (21, 35, or 70 mg SC)

* n=38, †n=39, ‡n=37

About Phase 2 Efficacy Estimand and Treatment Policy Estimand (Intent-to-Treat Analysis)

- The **efficacy estimand** represents the efficacy as if treated participants had adhered to MariTide for the entire 52-week study period. The efficacy estimand includes endpoint data so long as study drug is taken. Where endpoint data is missing with early discontinuation, the endpoint results for the patient are estimated using individual patient response and predicted performance after drug discontinuation.
- The **treatment policy estimand**, i.e., intent-to-treat analysis, represents the efficacy of treated participants regardless of adherence to MariTide for the entire 52-week study period and conforms to regulatory guidance for clinical trials. The treatment policy estimand includes all endpoint data, irrespective of whether study drug is taken or not. Where endpoint data is missing with early discontinuation, this approach assumes the endpoint for the study patient approximates that of placebo.
- The difference between the results generated by the efficacy estimand and the treatment policy estimand was driven by early discontinuations and a conservatively defined treatment estimand used in the Phase 2 study.