

Supplement to: Large multicenter randomized trials in autism: key insights gained from the balovaptan clinical development program

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Table S1. Primary and secondary efficacy objectives in the VANILLA, aV1ation, and V1aduct clinical trials.

Efficacy objective	Endpoint
VANILLA	
Primary efficacy objective	<ul style="list-style-type: none"> • Change from baseline at week 12 on the SRS-2
Secondary efficacy objective	<ul style="list-style-type: none"> • Change from baseline at week 12 in the Vineland™-II • Change from baseline at week 12 in the Vineland™-II, ABC, RBS-R, ADAMS, and STAI • Change from baseline at week 12 in the CGI-I and CGI-S • Clinical response (CGI-S score of 1 or 2*)
aV1ation	
Primary efficacy objective	<ul style="list-style-type: none"> • Change from baseline at week 24 on the Vineland™-II 2DC score
Secondary efficacy objective	<ul style="list-style-type: none"> • Change from baseline at weeks 12 and 24 on the Vineland™-II composite standard score • Change from baseline at weeks 12 and 24 in the Vineland™-II Communication, Socialization, and Daily Living Skills domains • Proportion of participants with a ≥6-point improvement in Vineland™-II 2DC score • Change from baseline at weeks 12 and 24 in the CGI-S and OACIS-S • Improvements in clinical impressions at weeks 12 and 24 as measured by the CGI-I and OACIS-I • Change from baseline at weeks 12 and 24 in the PedsQL™ Generic Core Scale • Change from baseline at weeks 12 and 24 in the Vineland™-II composite standard score in adults and children independently • Change from baseline at week 12 on the Vineland™-II 2DC
V1aduct	
Primary efficacy objective	<ul style="list-style-type: none"> • Change from baseline at week 24 on the Vineland™-II 2DC score
Secondary efficacy objective	<ul style="list-style-type: none"> • Change from baseline at week 12 on the Vineland™-II 2DC score • Change from baseline at weeks 12 and 24 in the Vineland™-II ABC standard score • Change from baseline at weeks 12 and 24 in the Vineland™-II Socialization, Communication, and Daily Living Skills domains • Change from baseline at weeks 12 and 24 in the PedsQL™ Core module summary and total scores • Change from baseline in CGI-S at weeks 12 and 24 • Improvements in CGI-I at weeks 12 and 24 • Change from baseline in the HAM-A total and domain scores at weeks 12 and 24 • Proportion of participants with a ≥6-point improvement in Vineland™-II 2DC score at weeks 12 and 24

*Protocol was revised to not include 25% improvement in the SRS-2 score as a measure of clinical response. 2DC, two domain composite; ABC, adaptive behavior composite; ADAMS, anxiety, depression, and mood scale; CGI-I, Clinical Global Impression Scale – Improvement; CGI-S, Clinical Global Impression Scale – Severity; HAM-A, Hamilton Anxiety Rating Scale; OACIS-I, Ohio Autism Clinical Impressions Scale – Improvement; OACIS-S, Ohio Autism Clinical Impressions Scale – Severity; PedsQL™, Pediatric Quality of Life Inventory; RBS-R, repetitive behaviors scale – revised; SRS-2, Social Responsiveness Scale, 2nd Edition; STAI, State-Trait Anxiety Inventory.