DTX301 Phase 1/2 Study in Ornithine Transcarbamylase (OTC) Deficiency

Cohort 2 and 3 Data Update

January 9, 2020

Legal Warning

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Up to Six of Nine Patients Responding Including 3 Female Responders

- Cohort 3: Responses from all three patients
  - Patient 7: Complete responder (off NH3 scavenger drugs and diet)
  - Patient 8: Responder (has not yet tapered medication and diet, still on steroids)
  - Patient 9: Potential responder (requires more follow-up past steroid treatment period)
- Cohort 2, Patient 6: Additional new female responder
  - Response began at Week 52 and was confirmed at Week 78
  - Started to taper alternate pathway medications and liberalize protein-restricted diet
- To date, three complete responders off all NH3 scavenger medications and diet
  - Sustained significant improvements in ureagenesis
  - Clinical and metabolically stable after discontinuing alternate medications and liberalizing protein-restricted diet

Responses Observed in All Dose Cohorts

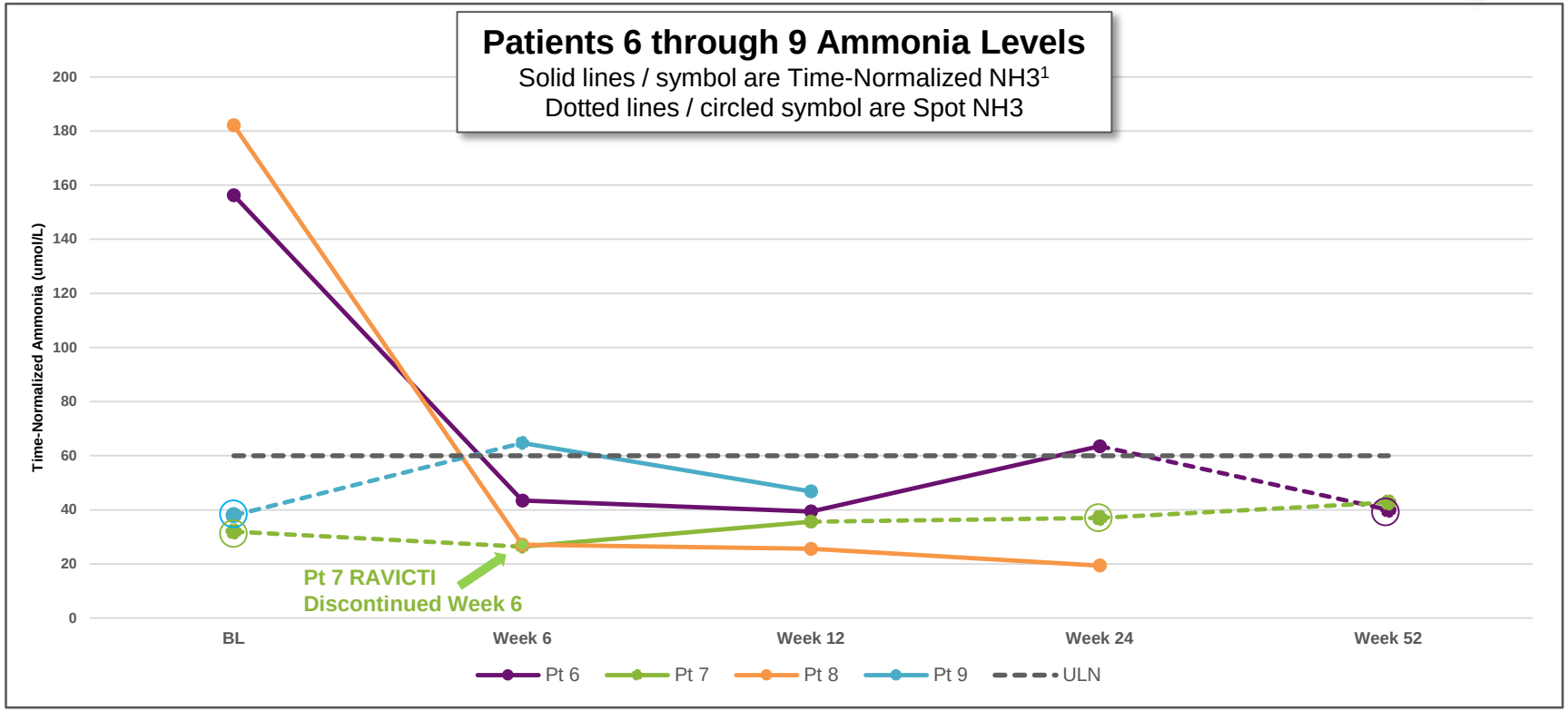
Up to 3 Responders at Cohort 3 Dose

Cohort / Dose (GC/kg)	Patient / Follow-Up Duration	Gender	% Change in Ureagenesis (baseline → after treatment, % normal[1])	% Change in Ammonia Levels (baseline → after treatment, umol/L)	Alternate Pathway Medication and Diet Status	Response Status
Cohort 1 (2e12 dose)	Patient 1 (Week 104)	M	**+81% (67% → 121%)**	Normal levels maintained	**Off medications Liberalized diet**	**Complete responder[3]**
	Patient 2 (Week 104)	F	+6% (52% → 55%)	**92% decrease (146 → 11)**	No change	No response (evaluating ammonia response)
	Patient 3 (Week 104)	M	**+81% (48% → 87%)**	Normal levels maintained	No change	No response (evaluating late ureagenesis response)
Cohort 2 (6e12 dose)	Patient 4 (Week 78)	M	**+79% (66% → 118%)**	Normal levels maintained	**Off medications Liberalized diet**	**Complete responder**
	Patient 5 (Week 78)	F	-38% (19% → 12%)	Normal levels maintained	No change	No response
	Patient 6 (Week 78)	F	**+218% (20% → 64%)**	**74% decrease (156 → 40)**	**Tapering medication Liberalizing diet**	**Responder (new)**
Cohort 3 (1e13 dose)	Patient 7 (Week 52)	F	**+79% (24% → 64% & 44%)**	Normal levels maintained	**Off medications Liberalized diet**	**Complete responder**
	Patient 8 (Week 24)	F	?%[2] (66% → 25%)	**90% decrease (184 → 19)**	No change yet	**Responder** (strong consistent ammonia reduction; clinical benefit noted; still on steroids)
	Patient 9 (Week 12)	M	**+123% (25%[4] → 56%)**	Normal levels maintained	No change yet	**Responder (potential)** (still on steroids; more time needed)

[1] Normal rate of ureagenesis = 300 umol*kg/hr
[2] Aberrant high baseline ureagenesis values inconsistent with patient clinical severity making ureagenesis not interpretable
[3] Complete responder = biochemical effect sustained after discontinuation of alternate pathway medications and diet liberalization
[4] Baseline ureagenesis based on screening value

Ammonia Levels Significantly Reduced or Controlled in Last 4 Patients

Including in Patient 7 after discontinuation of scavenger therapy at Week 6



1: Time normalized ammonia is defined as ammonia $AUC_{0\text{-}24\ hr}$ / 24hrs

DTX301 Safety Profile

- No infusion-related adverse events and no treatment-related serious adverse events
- All adverse events Grade 1 or 2
- All three patients in Cohort 3 had mild, clinically asymptomatic elevations in ALT levels, consistent with what has been observed in other AAV-based gene therapy programs
  - All have been responding to reactive tapering courses of steroids

Next Steps

- Enrolling three additional patients in prophylactic steroid cohort at 1e13 dose
  - Additional cohort was planned prior to Cohort 3 data based on benefit observed in other gene therapy studies and our own lab work
- Continuing discussions with FDA regarding potential Phase 3 study design
  - Ammonia expected to be a primary endpoint based on FDA feedback
  - Ureagenesis to be used as a measure of biologic activity that supports decision to taper alternative medications

Prophylactic steroid cohort (1e13 dose) update expected in second half of 2020

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