Treatment of Hypogonadal Men with Oral Testosterone Undecanoate (TU) Improves Psycho-Sexual, Well-Being and Body Composition Parameters

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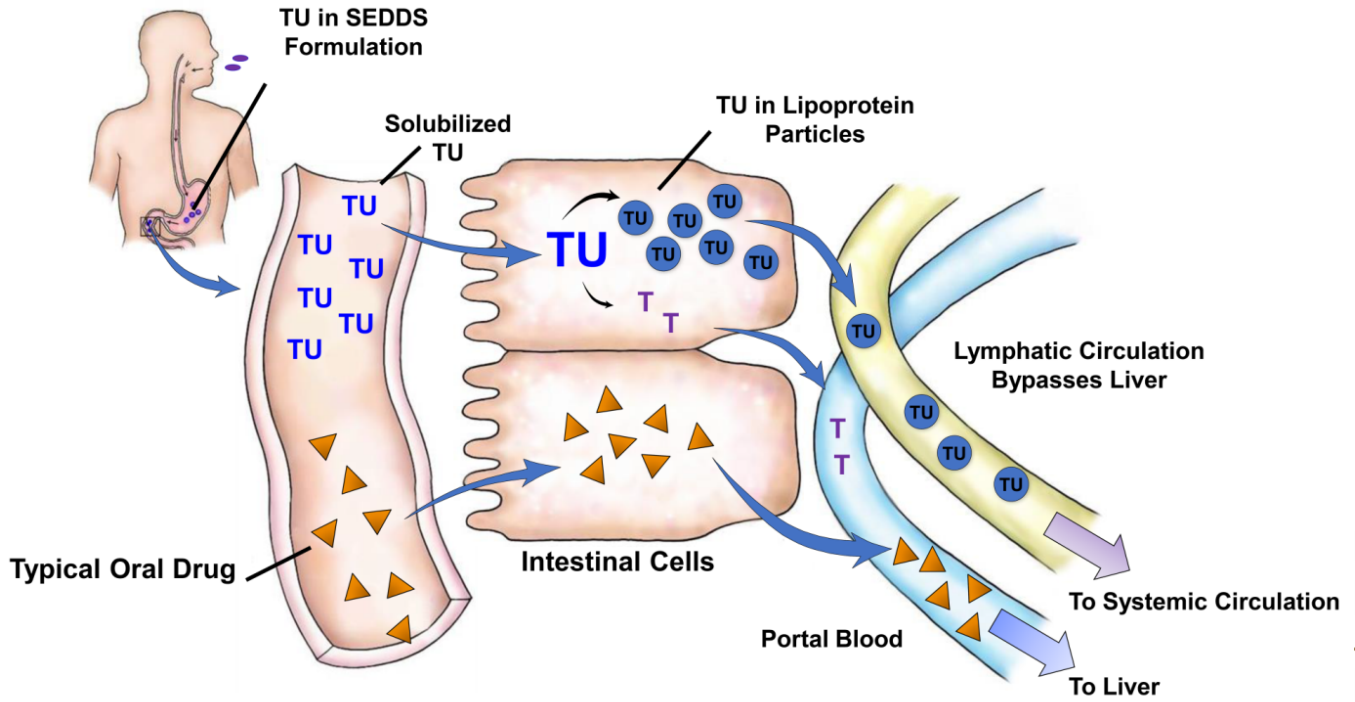
FDA-Approved Unique Oral TU Formulation for TRT in Hypogonadal Men

- Orally administered in a softgel capsule that constitutes a self-emulsifying drug-delivery system (SEDDS)[1]
  - Designed to promote the solubility, absorption, and subsequent bioavailability of TU[1]
- Highly lipophilic and absorbed via the intestinal lymphatics[1]
  - Avoids first-pass hepatic metabolism[1]
- No hepatotoxicity is observed with TU use[2]
- This proprietary formulation enhances the bioavailability of TU and reduces the impact of food on its absorption[1]



SEDDS, self-emulsifying drug-delivery system; T, testosterone; TRT, testosterone replacement therapy; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc. **2.** JATENZO [prescribing Information]. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019.

Objectives

- A new, oral testosterone replacement product, testosterone undecanoate (TU) oral capsules, was recently approved by the US FDA.
- **Evaluation of Secondary Endpoints:**
  - **Psycho-Sexual and General Well Being**
  - **Bone Mineral Density and Body Composition**

Methods

- Two clinical trials were conducted to evaluate, in part, the impact of TU on important secondary endpoints in hypogonadal men.
- Trial 1 was a 4-month study that investigates pharmacokinetics, safety variables, and certain symptom variables, such as changes the Psycho-sexual Daily Questionnaire (PDQ).
- Trial 2 was a 12-month study that investigates pharmacokinetics, safety variables, and certain symptom variables
  - Bone Mineral Density in the hip and spine
  - Changes in body composition, such as fat mass and lean mass
  - General Well-Being parameters

A Randomized, Open-label, Active-Controlled 4 -Month Phase 3 Trial (Trial 1)

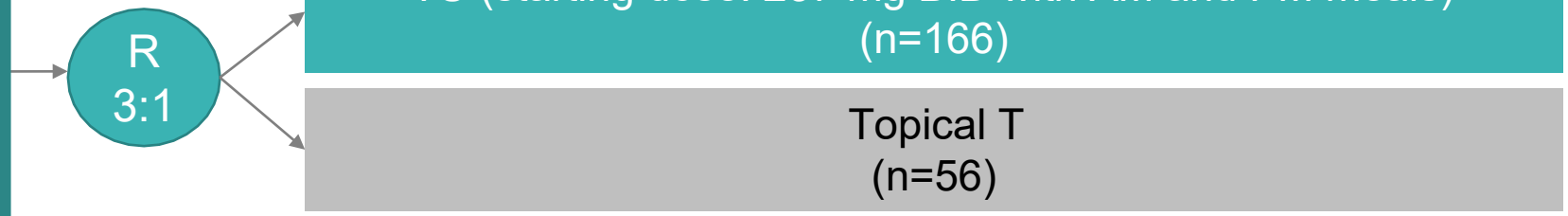
Patient Population (N=222)[1]

Key inclusion criteria

- Hypogonadal* men aged 18-65 years
- Signs/symptoms consistent with hypogonadism
- Naïve to TRT or washed out
- Stable doses of thyroid hormone and adrenal replacement hormones, if applicable

Key exclusion criteria

- Consistent with other TRT development programs



*Men aged 18 to 65 years old with a diagnosis consistent with the Endocrine Society guideline of 2 morning serum T levels <300 ng/dL and signs/symptoms consistent with hypogonadism.[1,2]

†Dose adjustments based on T C_{avg} from Visits 2 and 4; minimum and maximum doses were 158 mg BID and 396 mg BID, respectively.[1,2]

ABPM, automated blood pressure monitoring; BID, twice daily; C_{avg}, time-weighted average concentration; C_{max}, maximum observed concentration; DT, dose titration; PK, pharmacokinetics; R, randomization; T, testosterone; TRT, testosterone replacement therapy; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc. **2.** JATENZO [prescribing Information]. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019.

A Randomized, Open-label, Active-Controlled 12 -Month Phase 3 Trial (Trial 2)

- A phase 3 trial vs Topical T in hypogonadal men[1,*]

Patient Population (N=325)[1]

Key inclusion criteria

- Hypogonadal* men aged 18-75 years
- Naïve to TRT or washed out
- Stable doses of thyroid hormone and adrenal replacement hormones, if applicable

Key exclusion criteria

- Consistent with other TRT development programs

R 1:1

- Oral TU (starting dose T equivalent†: 200 mg BID with food) (n=162)
- Transdermal T-gel (starting dose of T: 50 mg once daily) (n=163)

*Men aged 18 to 75 years old with a diagnosis consistent with total serum T levels ≤300 ng/dL collected in the morning before 10:00 AM on 2 separate days within 2 weeks; †316 mg TU is equivalent to 200 mg T; ‡Dose adjustments based on T C_{avg} from visits on Day 30 and Day 60 at 4-6 hours post AM dose; minimum and maximum doses were 100 mg BID and 300 mg BID for oral TU and 25 mg daily and 100 mg daily for T-gel, respectively[1]; §Or Day105 for subjects given oral TU who had dose titration on Day 74; ‖Subject discontinued if repeated T value >1800 ng/dL

BID, twice daily; C_{avg}, time-weighted average concentration; C_{max}, maximum observed concentration; CV, cardiovascular; DT, dose titration; PK, pharmacokinetics; R, randomization; T, testosterone; TRT, testosterone replacement therapy; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc.

Patient Demographics

Characteristic	Trial 1		Trial 2	
	TU (n=166)	Topical T (n=56)	TU (n=161)	T Gel (n=160)
Age, Years				
Mean	51.6	53.4	55.0	54.9
Range	24-65	31-65	20-75	20-75
Race, %				
Asian	1.8	3.6	0.0	1.6
Black or African American	17.5	19.6	11.2	12.8
White	80.1	75.0	87.6	83.8
Other	0.5	0.0	1.2	1.9
Body Mass Index, kg/m^2				
Mean	31.8	30.9	30.0	29.88
Range	17-38	21-38	17.1-38.5	19.6-37.4
Baseline Clinical Characteristics, %				
Prediabetic	36.1	33.9	38.5	35.0
Diabetes Mellitus	24.1	26.8	19.3	20.0
Hypertensive	52.4	46.4	41.0	47.5

T, testosterone; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc.

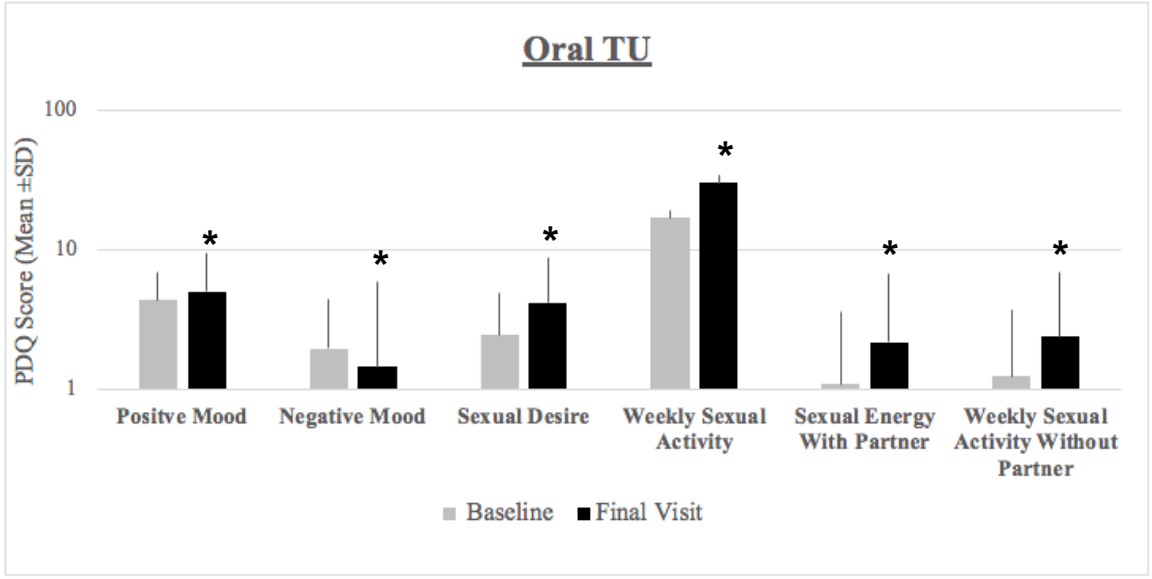
TU Total Testosterone C_{avg}

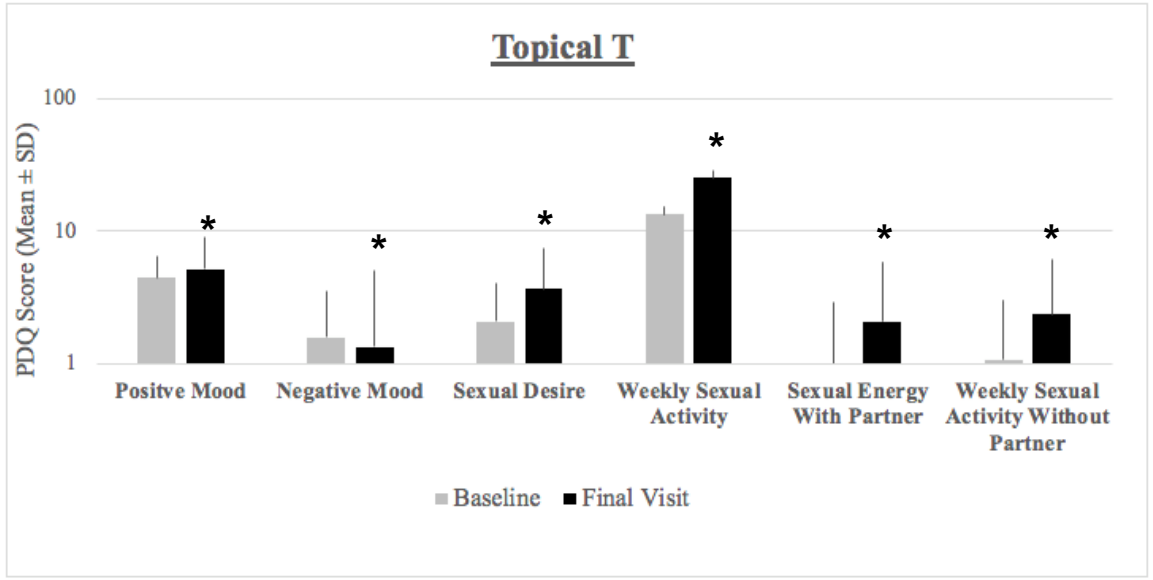
	Serum T C_{avg} (mean ± SD)	Serum T C_{avg} (mean ± SD)
Trial 1	TU = 489 ± 155 ng/dL	Topical T = 473 ± 169 ng/dL
Trial 2	TU = 524 ± 215 ng/dL	T Gel = 425 ± 178 ng/dL

C_{avg}, time-weighted average concentration; CI, confidence interval; T, testosterone; TU, testosterone undecanoate

1. Swerdloff R, et al. *Endocr Rev*. 2018;39(2) [supplement]. Poster E0010776. **2.** JATENZO [prescribing Information]. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019.

Trial 1: Effects of Oral TU Psychosocial Daily Questionnaire

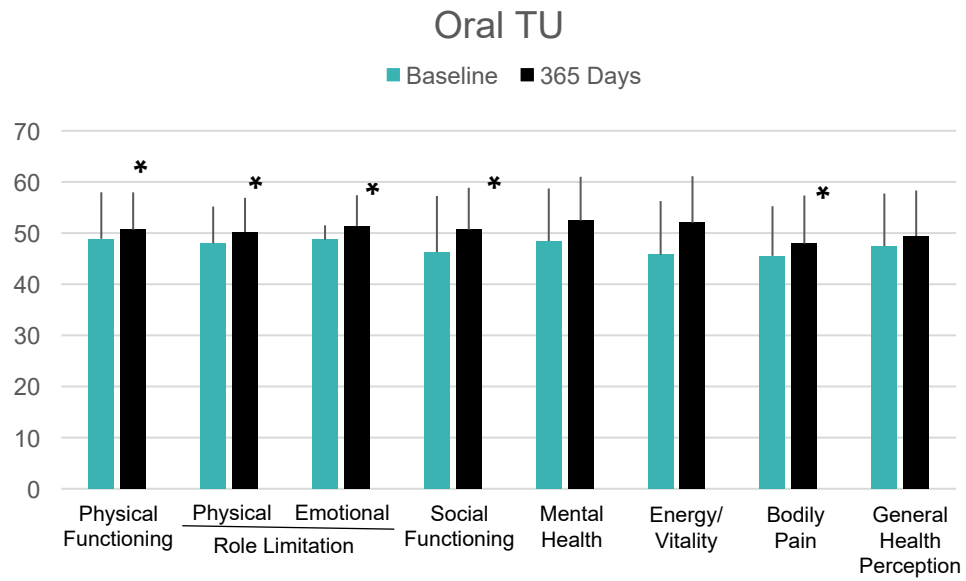


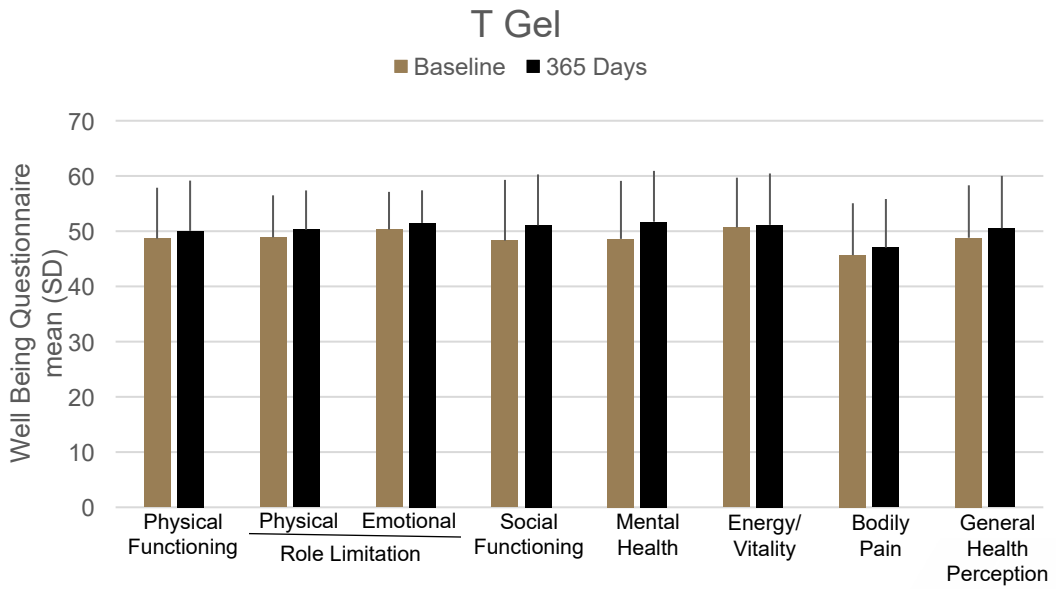


ANCOVA, analysis of covariance; CI, confidence interval; LS, least squares; SD, standard deviation; TU, testosterone undecanoate
* Denotes p < 0.05 when compared to baseline.
LS mean difference, 95% CI, and *P* values are based on ANCOVA model with change from baseline as the dependent variable, treatment group as a factor, and baseline value as the covariate

1. Data on file. Clarus Therapeutics, Inc.

Trial 2: Effects of Oral TU General (SF-36) Well-Being Parameters



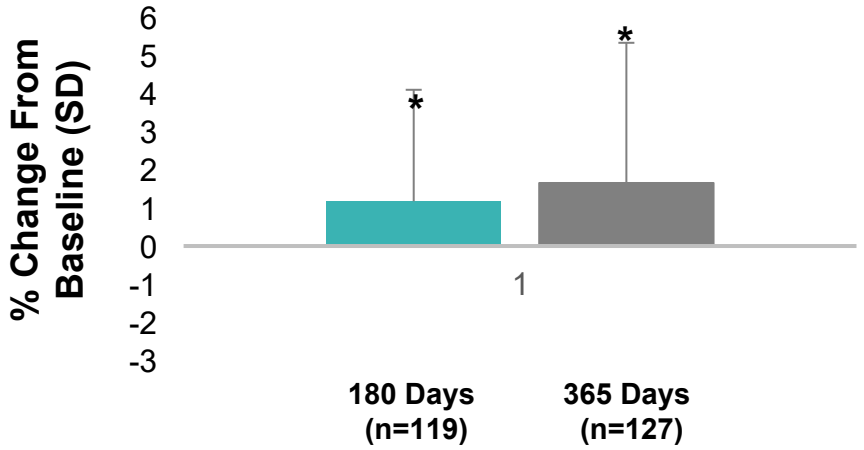


*Denotes statistical difference between the magnitude of improvement between TU and T Gel. All statistical differences showed a greater magnitude of increase for the TU group.
Treatment group, visit, and the interaction of treatment group and visit were included in the model as fixed effects, and subject was included as a random effect.

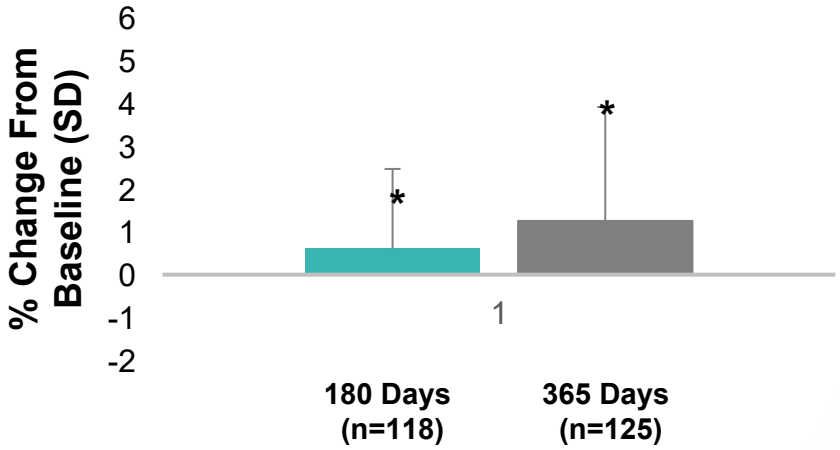
1. Data on file. Clarus Therapeutics, Inc.

Trial 2
Oral TU Effects on Bone Mineral Density

Percentage Change From Baseline in Patients Receiving Oral TU: **Spine** (±SD)



Percentage Change From Baseline in Patients Receiving Oral TU: **Hip** (±SD)

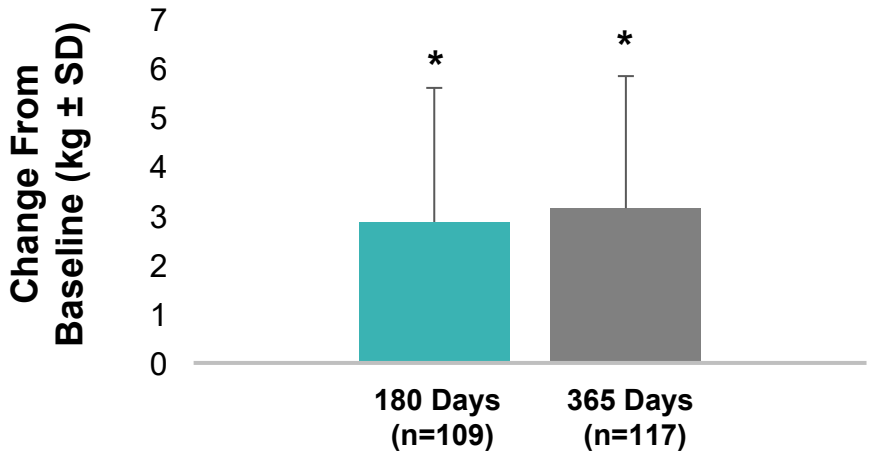


Only Trial 2 measured BMD because of study duration
* Denotes p < 0.001 versus baseline
SD, standard deviation; TU, testosterone undecanoate

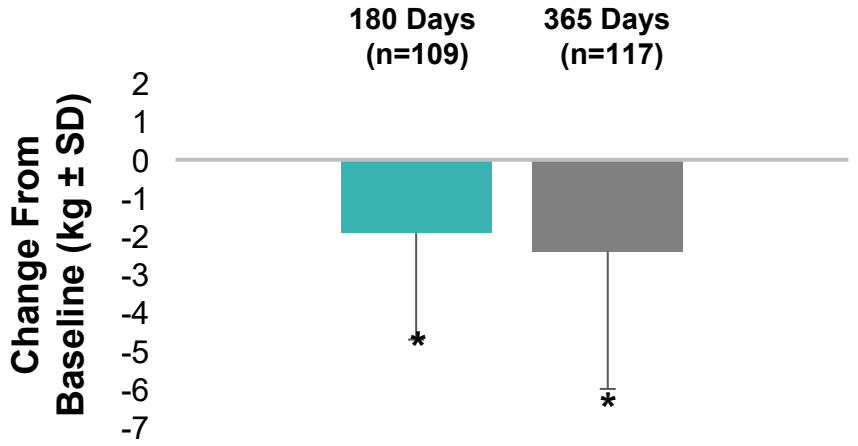
1. Data on file. Clarus Therapeutics, Inc.

Trial 2
Oral TU Effects on Lean Body Mass and Fat Mass

Lean Body Mass in Patients Receiving Oral TU: Change From Baseline (kg ± SD)



Fat Mass in Patients Receiving Oral TU: Change From Baseline (kg ± SD)

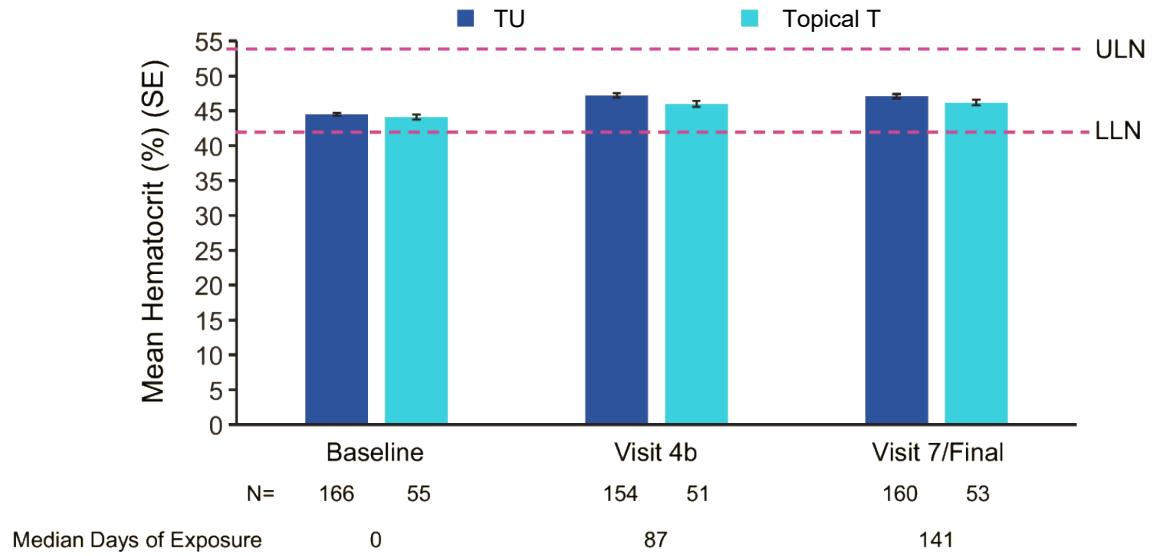


Only Trial 2 measured Body composition because it was long enough
* Denotes p < 0.001 compared to baseline.
kg, kilogram; SD, standard deviation; T, testosterone; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc.

Trial 1: Hematocrit Measurements

HCT Concentrations Increase With Testosterone Replacement[1]



Study Visit	Mean % Increase in HCT From Baseline[2]	
	TU (N=166)	Topical T (N=55)
Visit 4	6.41%	4.36%
Final visit*	5.97%	4.73%

- Overall incidence of HCT increase (>54%) with TU was 4.8%[2]
- 8 subjects on TU had an HCT >54% at some point in the study[2]
  - No clinical events were associated with these increases
  - No patient discontinued treatment because of elevated HCT

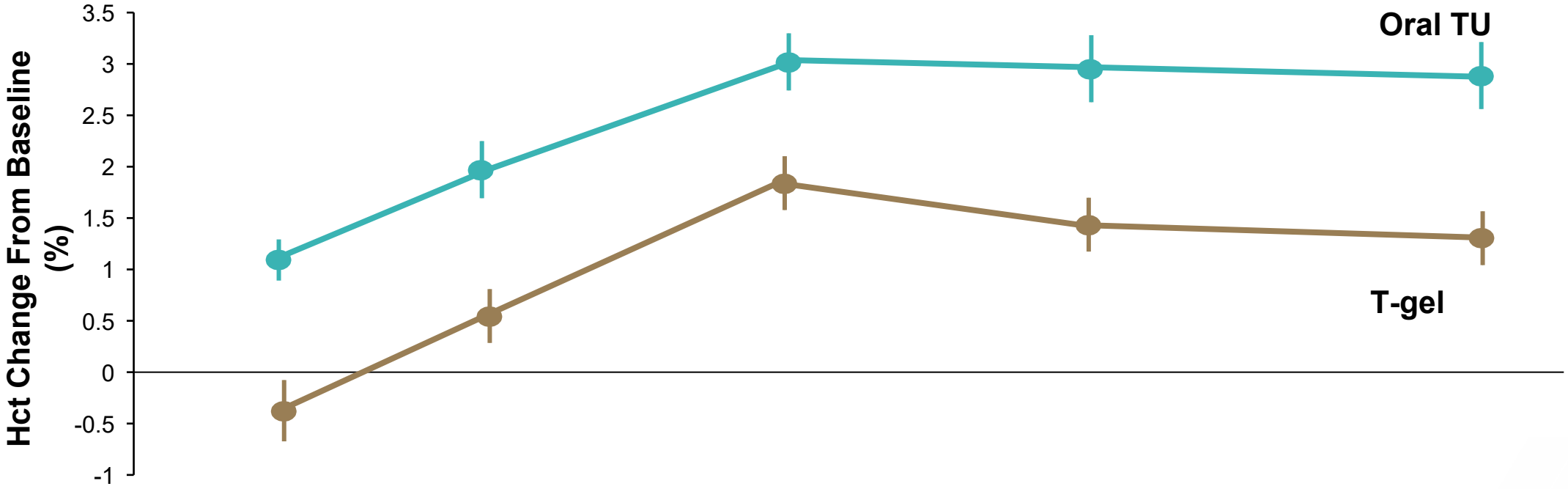
*Final visit was defined as either Visit 7 or date of last data collection if terminated early.[2]

HCT, hematocrit; LLN, lower limit of normal; SE, standard error; T, testosterone; TRT, testosterone replacement therapy; TU, testosterone undecanoate; ULN, upper limit of normal

1. Swerdloff R, et al. *Endocr Rev*. 2018;39(2) [supplement]. Poster E0010776. **2.** Data on file, Clarus Therapeutics, Inc.

Trial 2

Hematology: Change in hematocrit from baseline*

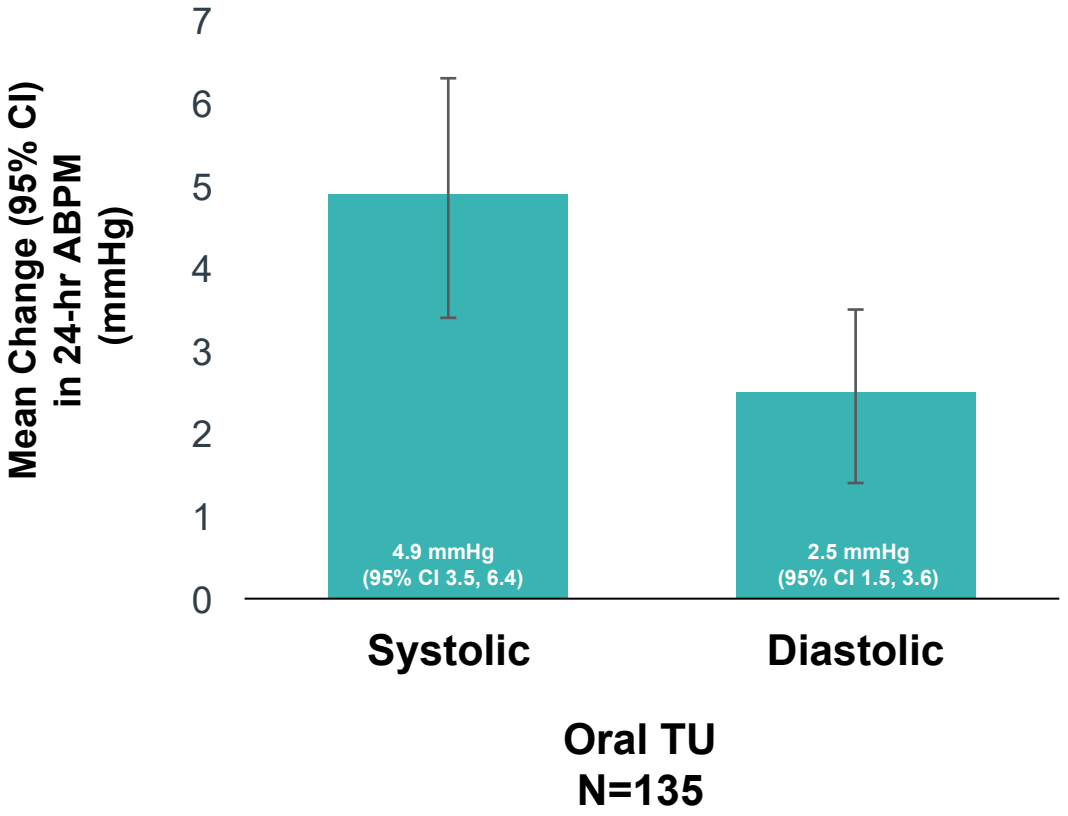


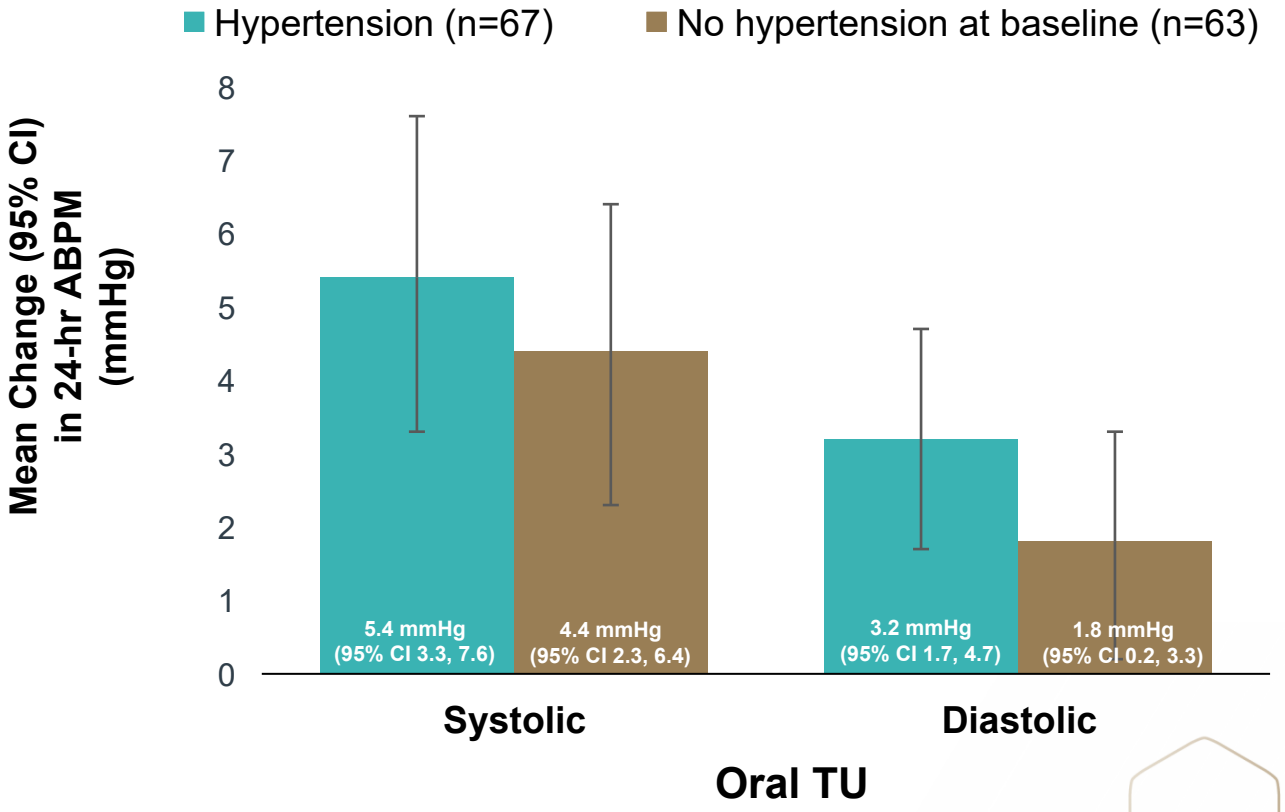
Study Day	30	90	180	270	365
Oral TU, N	156	143	136	132	127
T-gel, N	157	151	141	135	131

*For patients completing Day 365.
Hct, hematocrit; T, testosterone; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc.

Trial 1: Ambulatory Blood Pressure Monitoring and Hypertension with Oral TU



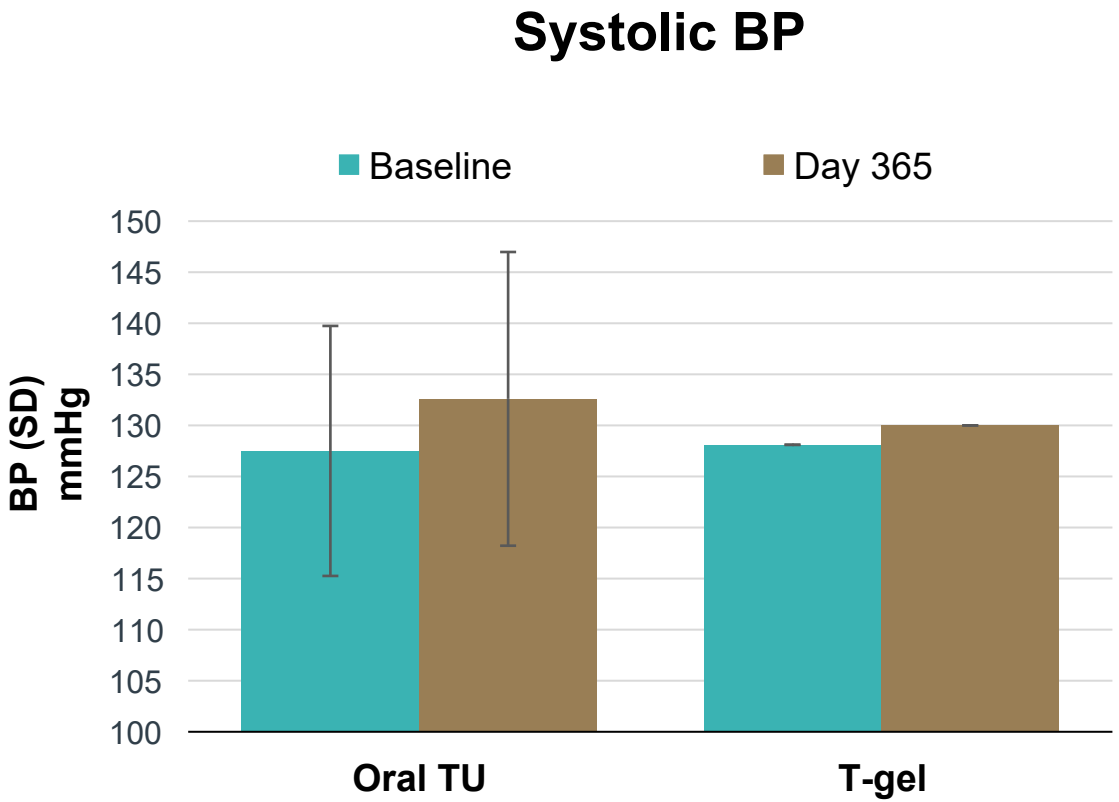


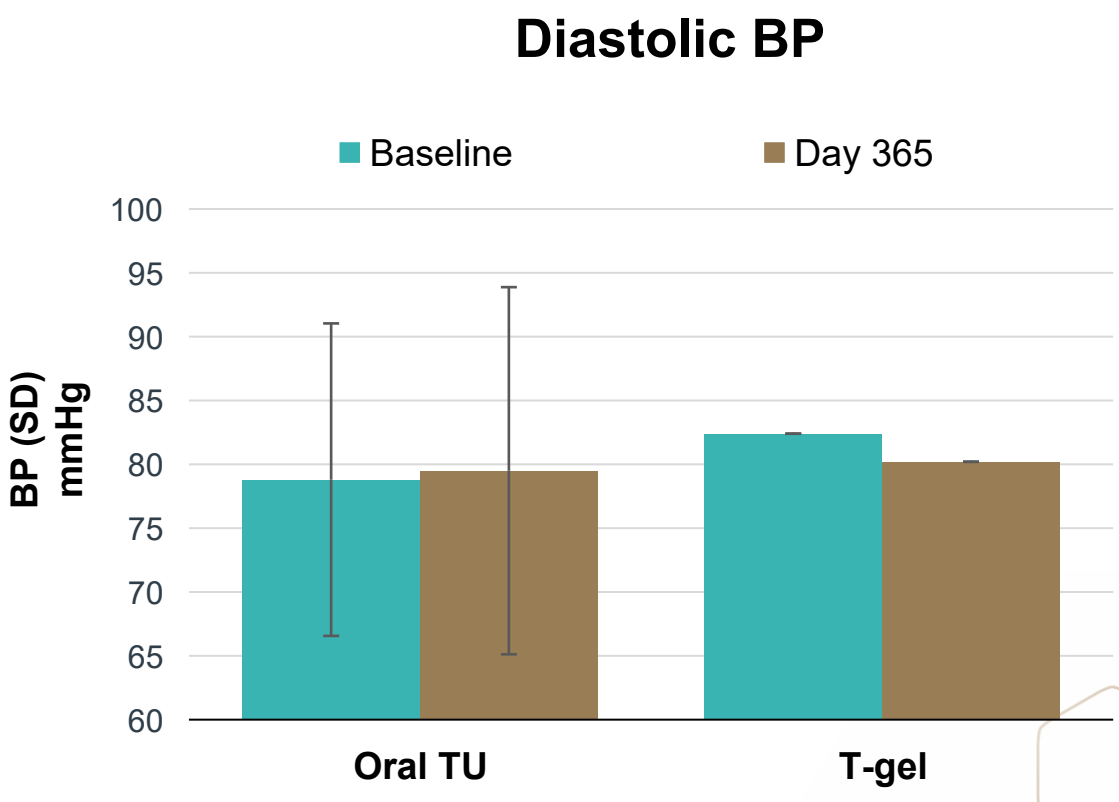
- During the study, 7.2% (n=12) of patients on JATENZO started antihypertensive drugs or had their antihypertensive regimen increased

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CI, confidence interval; n=total number of patients included in ABPM; mmHg, millimeters of mercury.

1. JATENZO [prescribing Information]. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019.

Trial 2: Safety Data
Effect of treatment on blood pressure





BP, blood pressure; T, testosterone; TU, testosterone undecanoate

1. Data on file. Clarus Therapeutics, Inc.

Liver Function Tests

Trial 1

Liver Enzyme Measurements	Change From Baseline to Final Visit*	
	TU (n=166)	Topical T (n=55)
ALT	–3.541 U/L	–4.078 U/L
AST	–0.365 U/L	–1.745 U/L
Bilirubin	–0.800 µmol/L	0.311 µmol/L

- No significant changes in liver function tests were observed in either treatment group

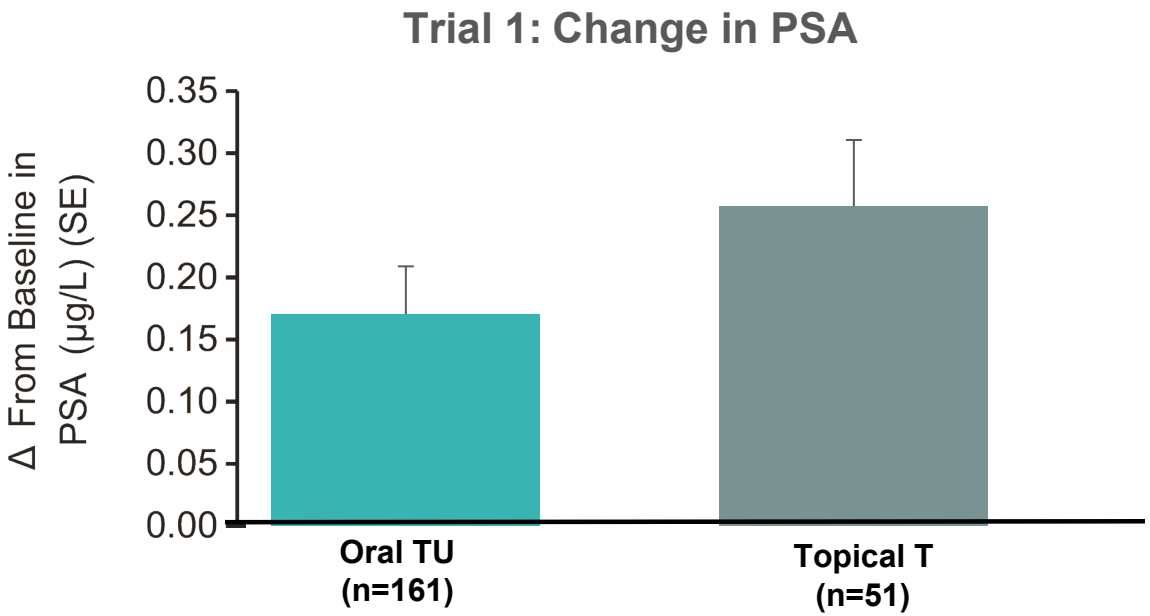
Trial 2

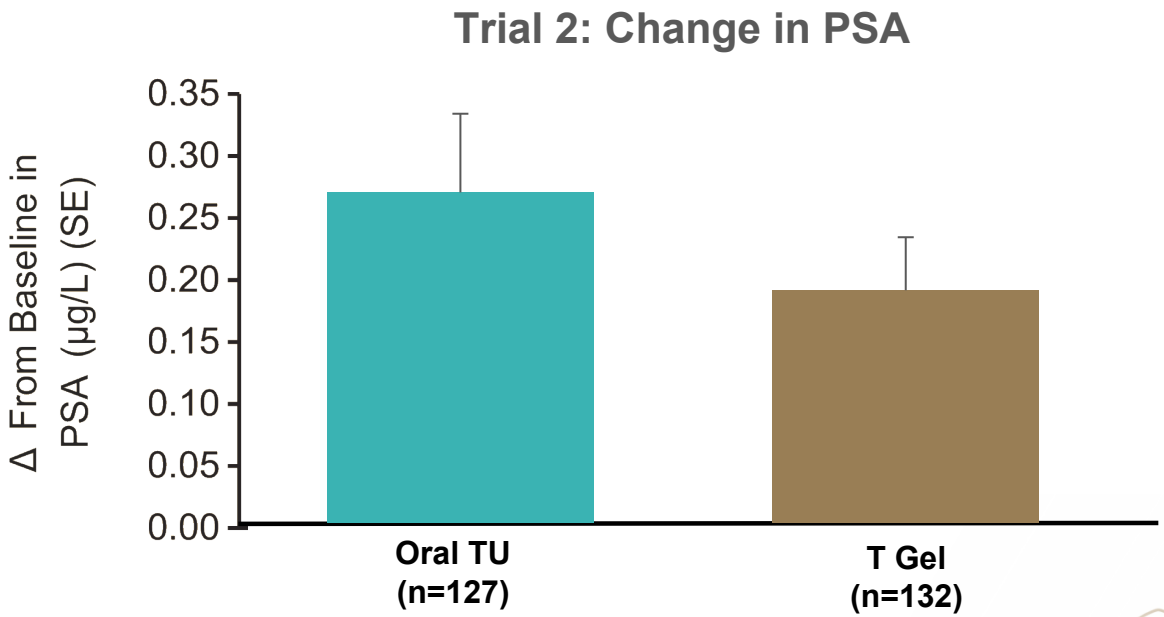
Liver Enzyme Measurements	Change From Baseline to Final Visit*	
	TU (n=161)	T Gel (n=159)
ALT	-2.286 U/L	-2.132 U/L
AST	0.677 U/L	-0.876 U/L
Bilirubin	0.010 µmol/L	-0.034 µmol/L

- No significant changes in liver function tests were observed in either treatment group

*Final visit was defined as either Visit 7 or date of last data collection if terminated early.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; T, testosterone; TU, testosterone undecanoate
1. Data on file, Clarus Therapeutics, Inc.

Change in PSA





PSA, prostate-specific antigen; T, testosterone; TU, testosterone undecanoate

1. Swerdloff R, et al. *Endocr Rev*. 2018;39(2) [supplement]. Poster E0010776. **2.** Data on file, Clarus Therapeutics, Inc.

Oral TU: Conclusions

- Treatment of hypogonadal men with **oral TU** yielded:
  - Total testosterone concentrations in the mid-eugonadal range
  - **Improvement in Secondary Endpoints in 2 Studies**

  - Improvement **psycho-sexual parameters**, as measured by the PDQ
  - Increase **bone mineral density** in both spine and hip in 12 month study

  - Increase in **lean mass** and a decrease in **fat mass** in 12 month study

- **Safety parameters** between oral TU and transdermal testosterone replacement products are **similar**.
- However, oral TU has black box warning for **increased BP**. BP should be checked at some point after starting therapy. Unclear if class effect or not.