Repros THERAPEUTICS INC

Androxal® Safety Data Update
September 16, 2013

Developing clinical stage small molecule therapeutics to treat hormonal and reproductive system disorders

Preliminary Summary of ZA-300

- All subjects have completed 6 months of Androxal treatment and assessments for safety
- Data not locked or fully audited

ZA-300 Protocol

- Secondary hypogonadal men
- Morning Testosterone < 300 ng/dL
- BMI between 25 to 42
- Initial dose of 12.5 mg Androxal
  - Up-titrated to 25.0 mg if Testosterone is < 450 ng/dL
- 6 Months of treatment
- 30 Sites

ZA-300 Population Summary

- 499 Subjects Enrolled
  - 12.5 mg (n = 234)
  - 25.0 mg (n = 265), these subjects experienced a morning Testosterone less than 450 ng/dL and were up-titrated
- Race/Ethnicity
  - 84.5% Caucasian (includes Hispanic ethnicity)
  - 11.3% African American
  - 4.2% Other
- Mean Age 49 years
- 33.7% Previous T Users
- Baseline Testosterone 212 ng/dL
- Mean BMI at baseline 33

ZA-300 Adverse Events (≥ 2%) by Incidence

PREFERRED TERM	ANDROXAL 12.5 MG (N=234) N (%)	ANDROXAL 25 MG (N=265) N (%)	OVERALL (N=499) N (%)
UPPER RESPIRATORY TRACT INFECTION	29 (12.4)	29 (10.9)	58 (11.6)
HEADACHE	15 (6.4)	18 (6.8)	33 (6.6)
MUSCLE SPASMS	9 (3.8)	11 (4.2)	20 (4.0)
FATIGUE	10 (4.3)	4 (1.5)	14 (2.8)
SINUSITIS	6 (2.6)	6 (2.3)	12 (2.4)
CONSTIPATION	4 (1.7)	7 (2.6)	11 (2.2)
INFLUENZA	7 (3.0)	4 (1.5)	11 (2.2)
POLLAKIURIA	6 (2.6)	5 (1.9)	11 (2.2)
HOT FLUSH	3 (1.3)	7 (2.6)	10 (2.0)
DIZZINESS	6 (2.6)	4 (1.5)	10 (2.0)

ZA-300 Drug Related Events by Incidence and Severity (> 1%)

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PREFERRED TERM	ANDROXAL 12.5 MG (N=234) N (%)	ANDROXAL 25 MG (N=265) N (%)	OVERALL (N=499) N (%)
HEADACHE	6 (2.6)	5 (1.9)	11 (2.2)
MILD	4 (1.7)	5 (1.9)	9 (1.8)
MODERATE	2 (0.9)	0 (0.0)	2 (0.4)
HOT FLUSH	3 (1.3)	5 (1.9)	8 (1.6)
MILD	3 (1.3)	4 (1.5)	7 (1.4)
MODERATE	0 (0.0)	1 (0.4)	1 (0.2)
MUSCLE SPASMS	4 (1.7)	2 (0.8)	6 (1.2)
MILD	3 (1.3)	1 (0.4)	4 (0.8)
MODERATE	1 (0.4)	1 (0.4)	2 (0.4)
INCREASED APPETITE	4 (1.7)	1 (0.4)	5 (1.0)
MILD	3 (1.3)	1 (0.4)	4 (0.8)
MODERATE	1 (0.4)	0 (0.0)	1 (0.2)
DIZZINESS	3 (1.3)	2 (0.8)	5 (1.0)
MILD	2 (0.9)	2 (0.8)	4 (0.8)
MODERATE	1 (0.4)	0 (0.0)	1 (0.2)
MOOD SWINGS	4 (1.7)	1 (0.4)	5 (1.0)
MILD	4 (1.7)	1 (0.4)	5 (1.0)
ACNE	4 (1.7)	1 (0.4)	5 (1.0)
MILD	3 (1.3)	1 (0.4)	4 (0.8)
MODERATE	1 (0.4)	0 (0.0)	1 (0.2)
FATIGUE	3 (1.3)	1 (0.4)	4 (0.8)
MILD	2 (0.9)	0 (0.0)	2 (0.4)
MODERATE	1 (0.4)	1 (0.4)	2 (0.4)

Investigator Assigned Relationship to Androxal of Definitely, Possibly or Probably-Related

ZA-300 Drug Related Events by Incidence and Severity (> 1%)

PREFERRED TERM	ANDROXAL 12.5 MG (N=234) N (%)	ANDROXAL 25 MG (N=265) N (%)	OVERALL (N=499) N (%)
OEDEMA PERIPHERAL	3 (1.3)	0 (0.0)	3 (0.6)
MILD	3 (1.3)	0 (0.0)	3 (0.6)
GLYCOSYLATED HAEMOGLOBIN INCREASED	3 (1.3)	0 (0.0)	3 (0.6)
MILD	1 (0.4)	0 (0.0)	1 (0.2)
MODERATE	2 (0.9)	0 (0.0)	2 (0.4)
PROSTATIC SPECIFIC ANTIGEN INCREASED	3 (1.3)	0 (0.0)	3 (0.6)
MILD	1 (0.4)	0 (0.0)	1 (0.2)
MODERATE	2 (0.9)	0 (0.0)	2 (0.4)
WEIGHT INCREASED	3 (1.3)	0 (0.0)	3 (0.6)
MILD	2 (0.9)	0 (0.0)	2 (0.4)
MODERATE	1 (0.4)	0 (0.0)	1 (0.2)
RASH	0 (0.0)	3 (1.1)	3 (0.6)
MILD	0 (0.0)	3 (1.1)	3 (0.6)

Investigator Assigned Relationship to Androxal of Definitely, Possibly or Probably-Related

ZA-300 Events Causing Discontinuation

Subject ID	Androxal Dose	Preferred Term	Relationship
06-006	12.5mg	Muscle Spasms	Possibly
06-027	12.5mg	Paraesthesia/Muscle Spasms	Possibly
06-028	12.5mg	Aggression	Possibly
06-039	12.5mg	Constipation	Possibly
07-062	12.5mg	Vitreous Floaters	Defintley Not Related
12-045	12.5mg	Abdominal Pain/Flank pain/Epididymitis/Prostatitis	Possibly
12-075	12.5mg	Visual Impairment	Probably Not Related
12-083	12.5mg	Weight increased/Fatigue/Libido Decreased/Myalgia/Vision Blurred	Probably Not Related
16-001	12.5mg	Vision blurred/Nausea/Chest Pain/Dizziness/Headache/Dyspnoe	Possibly
17-017	12.5mg	Pre-existing Seminoma	Defintley Not Related
17-021	12.5mg	Hot flush/ED/Weight increased/Mood swings	Probably
17-048	12.5mg	URTI	Probably
18-011	12.5mg	Prostatic specific antigen increased	Not Specified
22-052	12.5mg	Increased appetite/Headache	Possibly
23-022	12.5mg	Fatigue/Weight increased/Change in sustained attention	Possibly
24-038	12.5mg	Diplopia	Probably
26-008	12.5mg	HIV test positive	Not Specified
30-041	12.5mg	Vision blurred	Possibly
02-001	25mg	Pollakiuria	Probably
02-029	25mg	DVT/Pulmonary Embolism	Possibly
15-004	25mg	Weight increased	Probably Not Related
15-037	25mg	Myalgia/Paraesthesia	Not Specified
16-023	25mg	Lethargy	Not Specified
17-016	25mg	Depression/Weight increased	Not Specified
19-005	25mg	Hot flush/Breast Enlargement/ED/Testicular atrophy	Possibly
30-047	25mg	Hepatic enzyme increased	Not Specified
43-024	25mg	Rosacea/thrombophlebitis	Possibly
43-042	25mg	Irritability	Possibly

Queries are outstanding for events missing relationship determination.

ZA-300 SAEs

Subject Numbe	Dose	Event Term	Relationship
06-042	12.5 mg	Hypotension/Bradycardia post Knee Replacement Surgery	Not Related
07-052	12.5 mg	Gallstone/Cholecystectomy	Not Related
12-071	12.5 mg	Biliary Colic/Common Bile duct dilatation	Not Related
14-080	12.5 mg	TIA	Not Related
15-003	12.5 mg	Food Poisoning	Not Related
16-001	12.5 mg	Chest pain/Shortness of breath	Not Related
16-029	12.5 mg	Cellulitis	Not Related
17-007	12.5 mg	Deep vein thrombosis temporally related to flight	Not Related
17-017	12.5 mg	Pre-existing Seminoma Left Testicle	Not Related
02-029	25 mg	Deep vein thrombosis/Pulmonary embolism	Possibly Related
06-034	25 mg	Atrial flutter	Not Related
07-002	25 mg	Diverticulitis	Not Related
19-007	25 mg	Cellulitis secondary to dog bite	Not Related
19-016	25 mg	Diverticulitis	Probably Not Related
22-001	25 mg	Bladder diverticulum/Kidney infection	Unlikely

ZA-300 PSA

- 37 subjects (7.4%) experienced an increase in PSA of more than 0.75 at the last assessment on Androxal
  - There was no difference in the incidence of PSA elevations by dose ($p = 0.6438$)
- No subjects required biopsy
- Most subject's PSA decreased once therapy was discontinued and testosterone subsequently decreased
- Elevated PSA is a pharmacological response to elevated T and not an adverse drug effect

ZA-300 Testosterone Response

- Over 90% of subjects had a maximum morning Testosterone above 300 ng/dL
- Almost 67% of subjects had a maximum morning Testosterone above 450 ng/dL
- 53% of subjects were up-titrated (T < 450 ng/dL)
- Only 3 subjects experienced a maximum morning Testosterone above 1,040 ng/dL (1720, 1479, 1264)
  - Two subjects reported concomitant testosterone replacement use
  - LH values of third subject suggest concomitant testosterone use
- Subjects who required up-titration were less-likely to respond to treatment
  - 13.6% of subjects treated with 25 mg had a maximum morning Testosterone less than 300 ng/dL
  - 3.6% of subjects treated with 12.5 mg had a maximum morning Testosterone less than 300 ng/dL

ZA-300 Summary

- Androxal was found to be well-tolerated
- Testosterone levels are restored to normal in a large majority of subjects
- Only one SAE (DVT/Pulmonary Embolism) was deemed possibly related to study medication by the Investigator
  - Causality may be associated with increased Testosterone rather than Androxal
  - Subject had multiple risk factors: obesity, hypertension, race, tall stature, height, family history of clotting disorder
- Overall safety profile is similar, if not superior, to testosterone replacements