Repros Therapeutics

Development of small molecule drugs for major unmet medical needs that treat male and female reproductive disorders.

Repros Disclaimer

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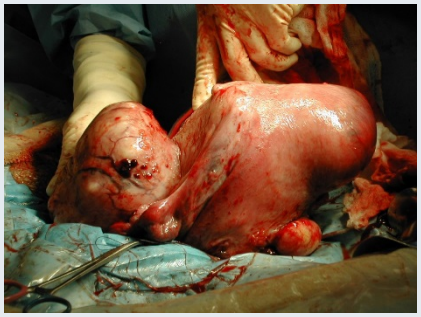
In this presentation, we rely on and refer to information and statistics regarding the pharmaceutical industry. We obtained this information and these statistics from third-party sources, which we have supplemented where necessary with information from publicly available sources and our own internal estimates. Industry publications and surveys generally state that they have obtained information from sources believed to be reliable, but do not guarantee the accuracy and completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified such data, and we make no any representation as to the accuracy of such information. Similarly, we believe our internal research is reliable, but it has not been verified by any independent sources.

Proellex

Addressing significant unmet female reproductive disorders

Uterine Fibroids & Endometriosis

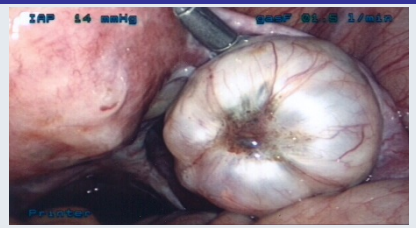
Poor therapeutic options for debilitating female disorders experienced by women in the prime of their life



Uterus Exhibiting Multiple Fibroids

Courtesy of Jay Goldberg, MD, MSCP
Director, Jefferson Fibroid Center
Director, Division of General OB/GYN
Jefferson Medical College, Philadelphia, PA

- Benign, monoclonal, hormone sensitive, smooth muscle tumors of the uterus
- Most common tumor of the female reproductive tract
  - Heavy bleeding / anemia
  - Abdominal pressure / pain / urinary frequency
- Affect 20-77% of women age 35 – 55
- 600,000 hysterectomies conducted annually

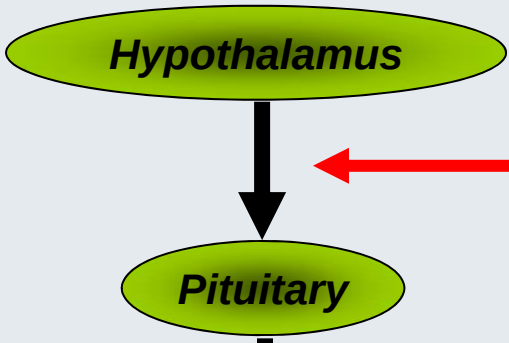


Endometrial lesions in peritoneum of woman suffering with endometriosis
Courtesy of Bruce A. Lessey, MD, PhD

- **Definition: the presence of epithelial and stromal endometrial cells outside of the uterine cavity**
- **Complaints of infertility or pregnancy loss**
- **Pelvic pain/back pain**
- **Dyspareunia (pain during sex)**
- **Dysmenorrhea (menstrual cycle cramps)**

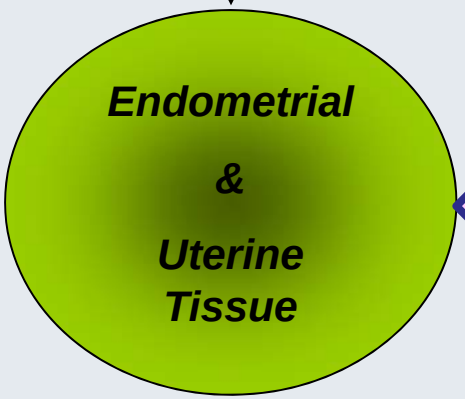
- **5% of women of reproductive age**
- **Estimated that 25 - 40% (2 – 4 million) of infertility cases may be due to endometriosis**
- **71 - 87% in women with chronic pelvic pain**
- **53% of teenagers with dysmenorrhea**
- **Many women have it without the diagnosis**
- **Unmet medical need**
  - **Oc's, Lupron, Danazol**
  - **Laparascopic procedures**
- **High recurrence rate after treatment**

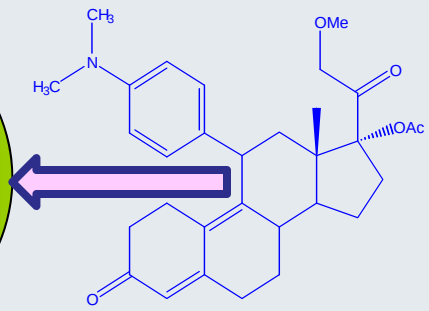
How Antiprogestins Like Proellex Work



Different than GnRH agonists and antagonists. These agents:

- ***Block hypothalamus / pituitary axis***
- ***Shut down hormonal secretions***
- ***Long-term side effects include bone loss***





Proellex

Antiprogestins

- **Selectively block progesterone activity**
- **Allow tonic hormone secretions**
  - **Alleviate negative side effects of GnRHa**
- **Potential for chronic use**

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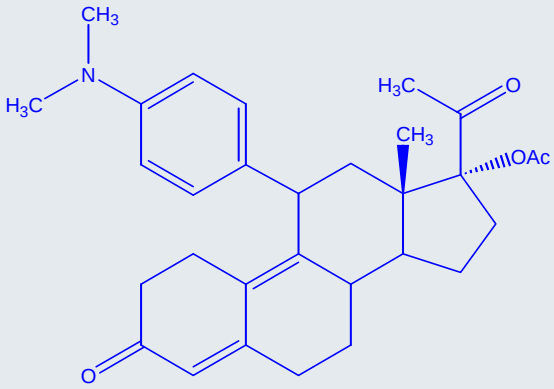
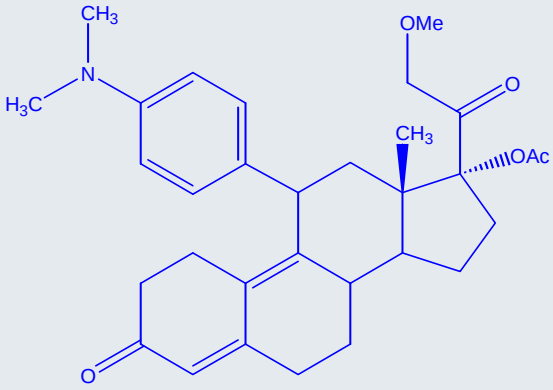
PROELLEX
EVOLUTION OF LEAD COMPOUND





CDB-2914 (Ulipristal Acetate)

- ***NIH precursor to Repros class***
- ***Allergan marketing molecule (Esmya) in Europe for treatment of uterine fibroids***

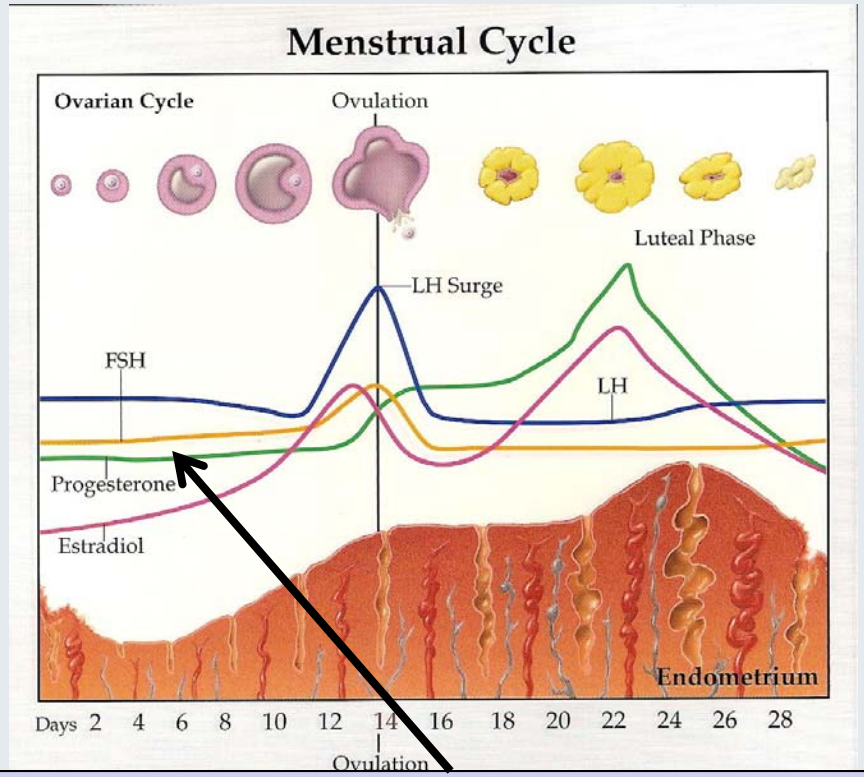
CDB-4124
Proellex (telapristone acetate)

- ***Repros worldwide exclusive license from NIH***
- ***Composition of matter patent***

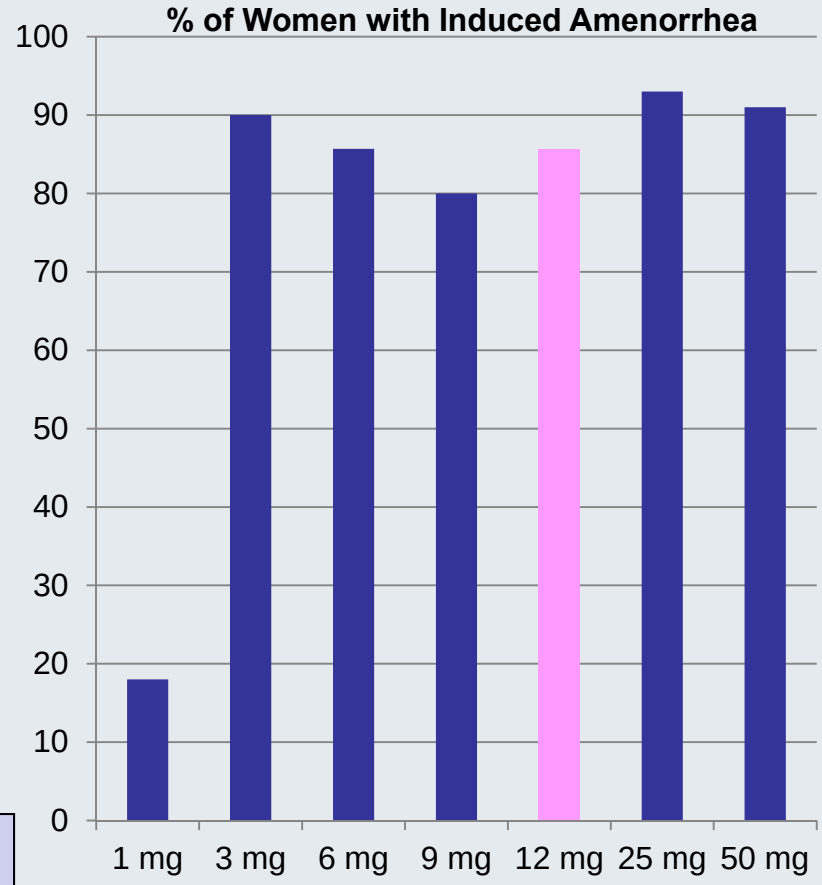
44 Analogues Synthesized to Date

An Effective Dose of Proellex Stops Menstruation in Majority of Women

Induction of amenorrhea relieves key symptoms of uterine fibroids and endometriosis

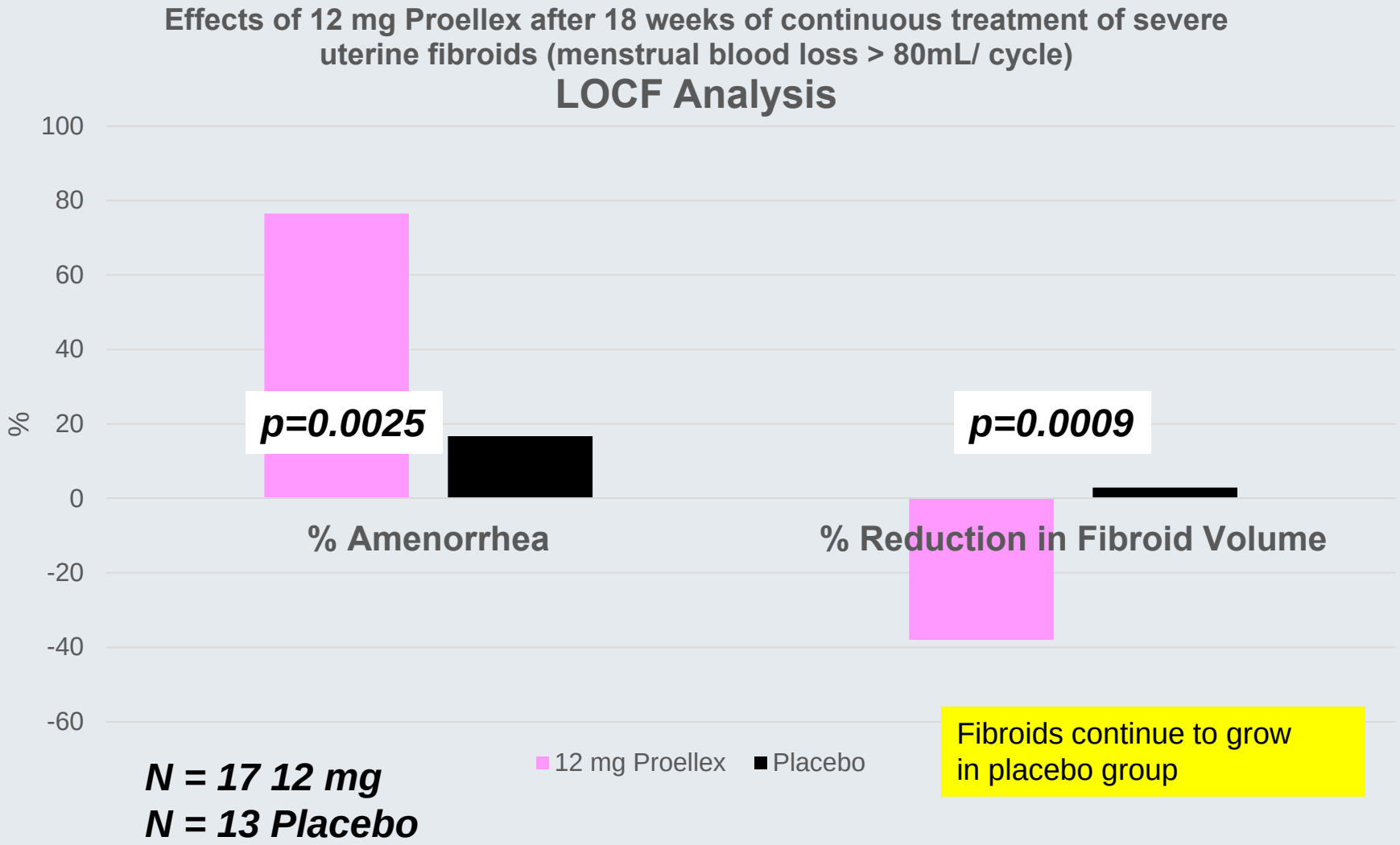


Proellex induced amenorrhea (no ovulation)
Mimics early follicular phase without progesterone while maintaining tonic estrogen levels
Unlike GnRh agonists/antagonists – no bone loss

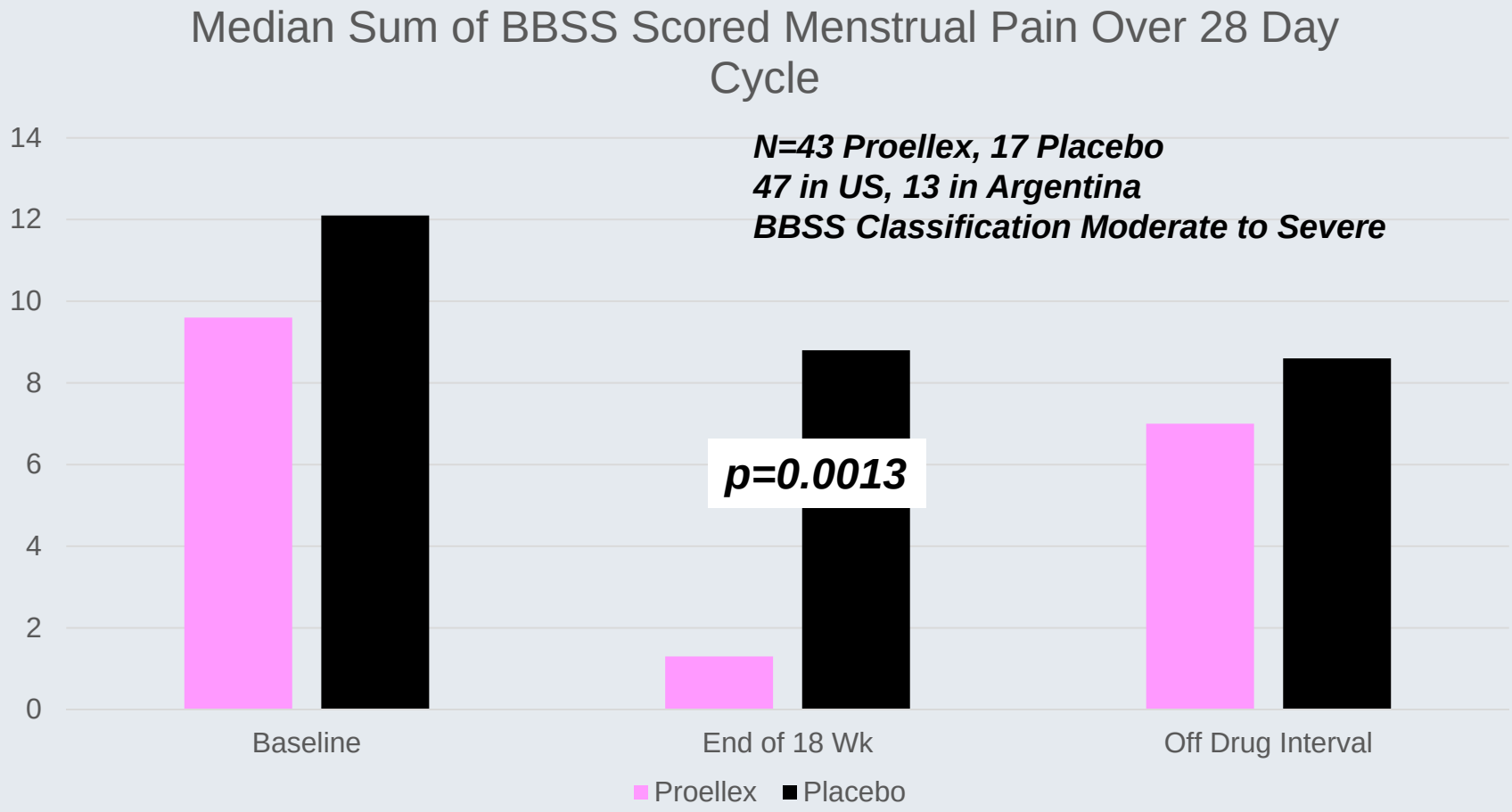


12 mg oral dose to be proposed to FDA for Phase 3 for both uterine fibroids and endometriosis

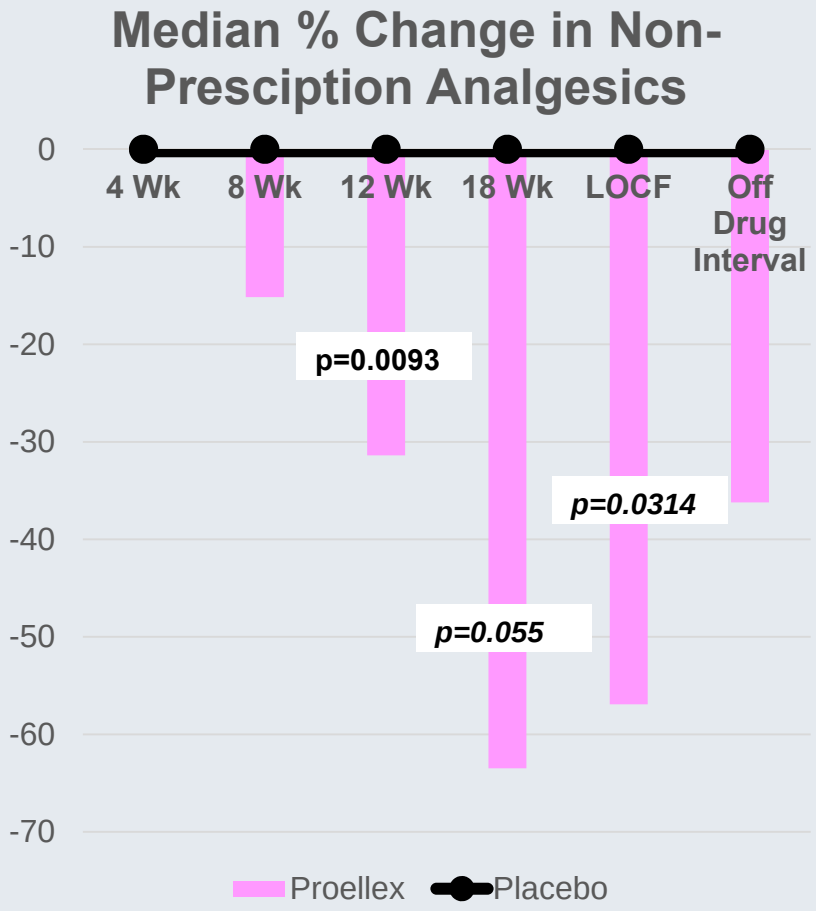
Impact of Proellex Treatment on Uterine Fibroids

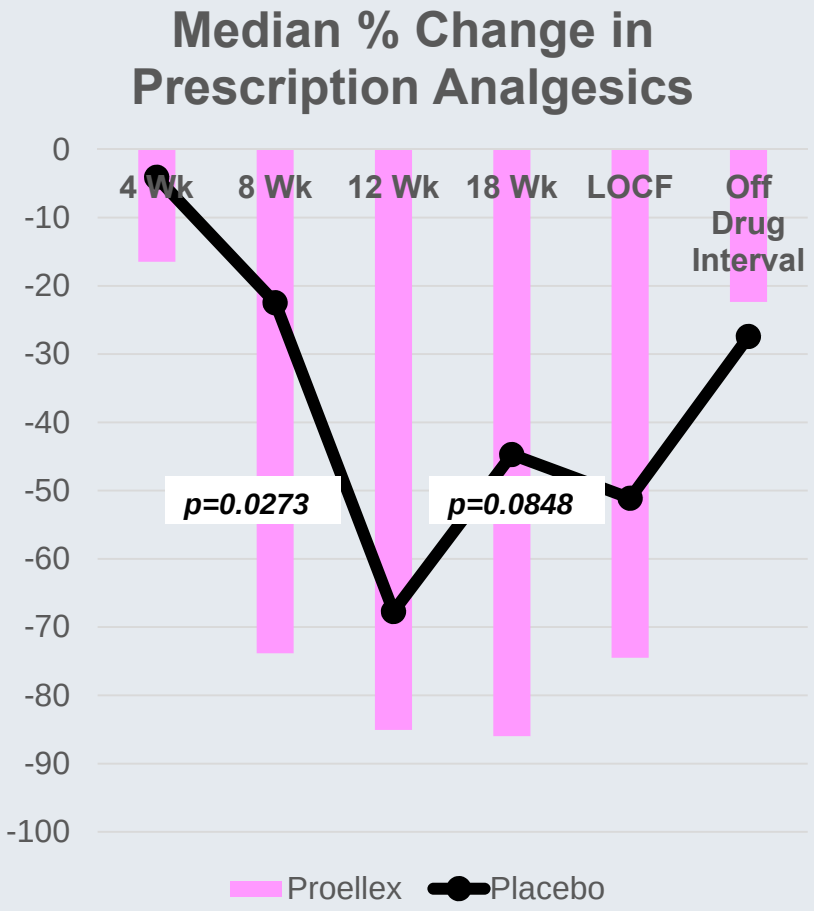


Impact of Proellex Treatment on Endometriosis



Impact of Proellex Treatment on Endometriosis

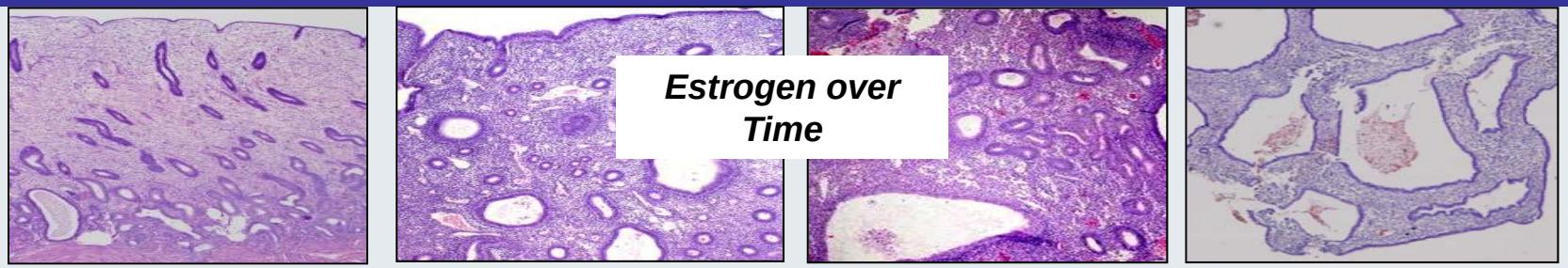




Baseline Analgesic Use Per 28 Day Menstrual Cycle

	Prescription	*Non-Prescription*
Proellex	***23.14 (40.81)***	***30.28 (74.96)***
Placebo	***14.38 (17.78)***	***18.94 (29.05)***

Key Advantage of Proellex Over Other Antiprogestins in Development



Proliferative → *Disordered Proliferative* → *Benign Endometrial Hyperplasia*

12.5mg Proellex No hyperplasia

Mutter et al, 2007

- *Required off Drug Interval to allow for:*
- *Menses*
  - *Refresh the endometrium*
    - *Potential unexpected uterine hemorrhage*
  - *Menses returns in 25-35 days*
- *Return of symptoms after cessation of treatment*

All other antiprogestins in development require off-drug-interval after 12 weeks of treatment

Proellex provides 18 weeks of significant symptom relief before Off-Drug-Interval

Proellex Clinical Goals

- Confirm Phase 3 requirements with FDA
  - Uterine Fibroids: Request Mtg. Q4-’16
  - Endometriosis: Request Mtg. Q4-’16
- Completed Proellex NDA components
  - Pre-clinical complete (including 2 carcinogenicity studies)
  - Manufacturing complete (API sourced, stable final drug product)
  - Phase 1 complete except TQtc
    - No signal in pilot study

Proellex Summary

- Potential Proellex market opportunity > $1 Billion for Fibroids and Endometriosis
- Rigorous clinical program working to move into Phase 3
- Significant clinical advantages identified against GnRH agonists/antagonists
- Longer symptom relief established against other approved or in development anti-progestins

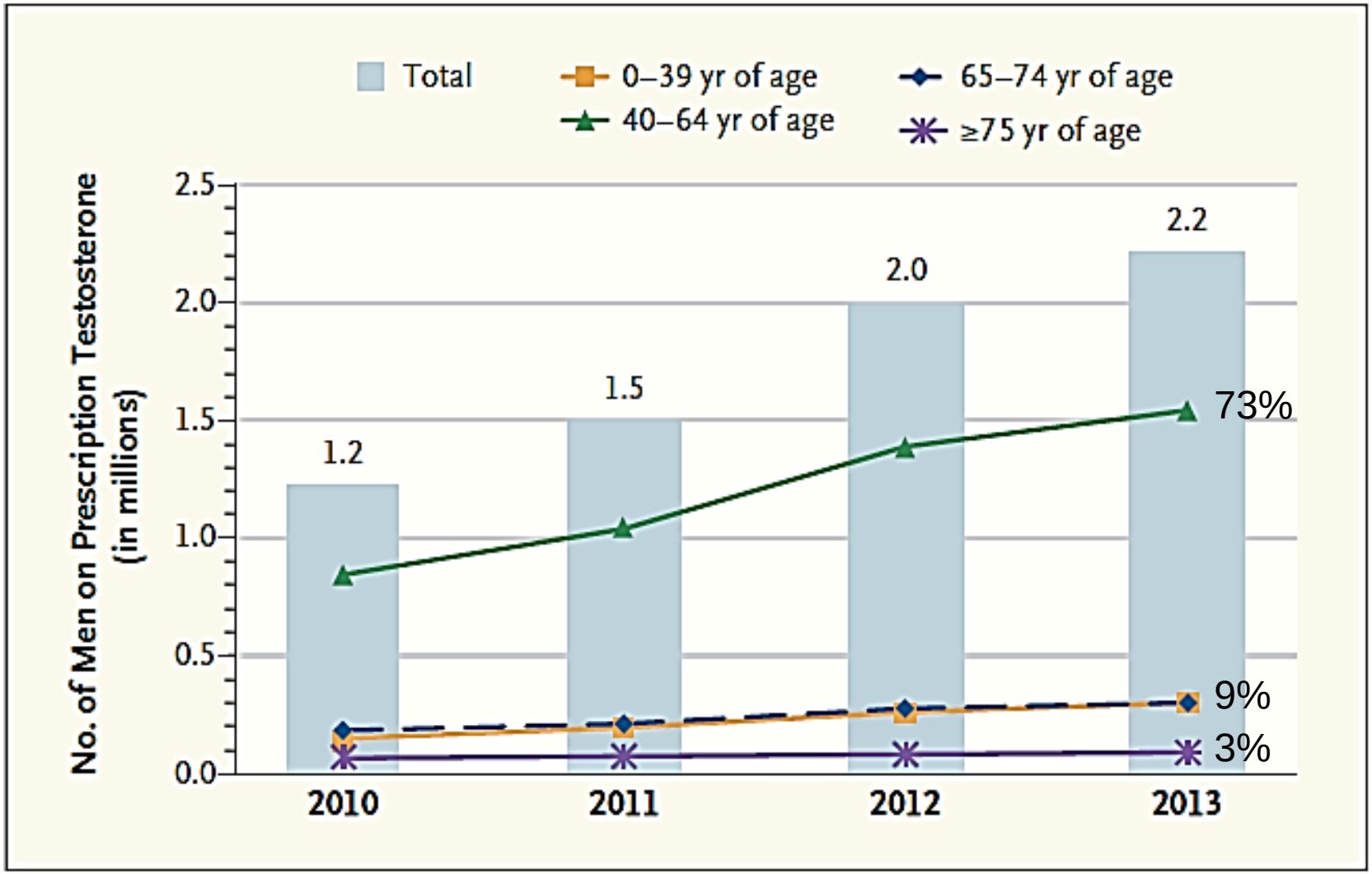
Encyzix (enclomiphene)

Rational treatment for secondary hypogonadism

Enclomiphene Development Status

- Central EU filing ongoing for treatment of secondary hypogonadism
  - Anticipated marketing authorization Q4-'17
- Repros to present as sponsor at 12/6/16 FDA Adcom
  - "Agenda: The committee will discuss appropriate clinical trial design features, including acceptable endpoints for demonstrating clinical benefit, for drugs intended to treat secondary hypogonadism while preserving or improving testicular function, including spermatogenesis."
  - No T replacement to be discussed due to negative effects on testicular function
- US Phase 2 "Proof of Concept" to evaluate clinical benefit
  - We plan to pursue Type C meeting with FDA when meaningful clinical benefit is identified

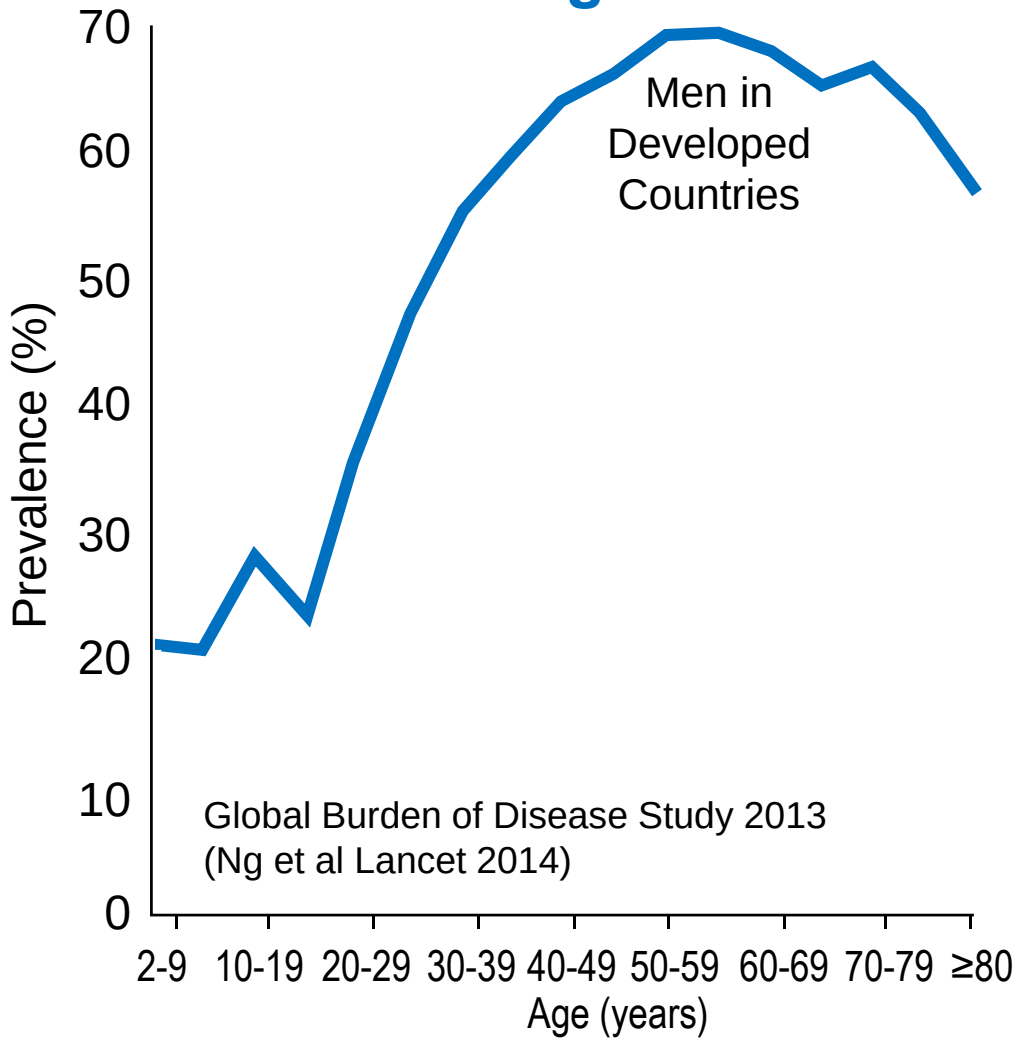
Prescription Claims for Testosterone Products



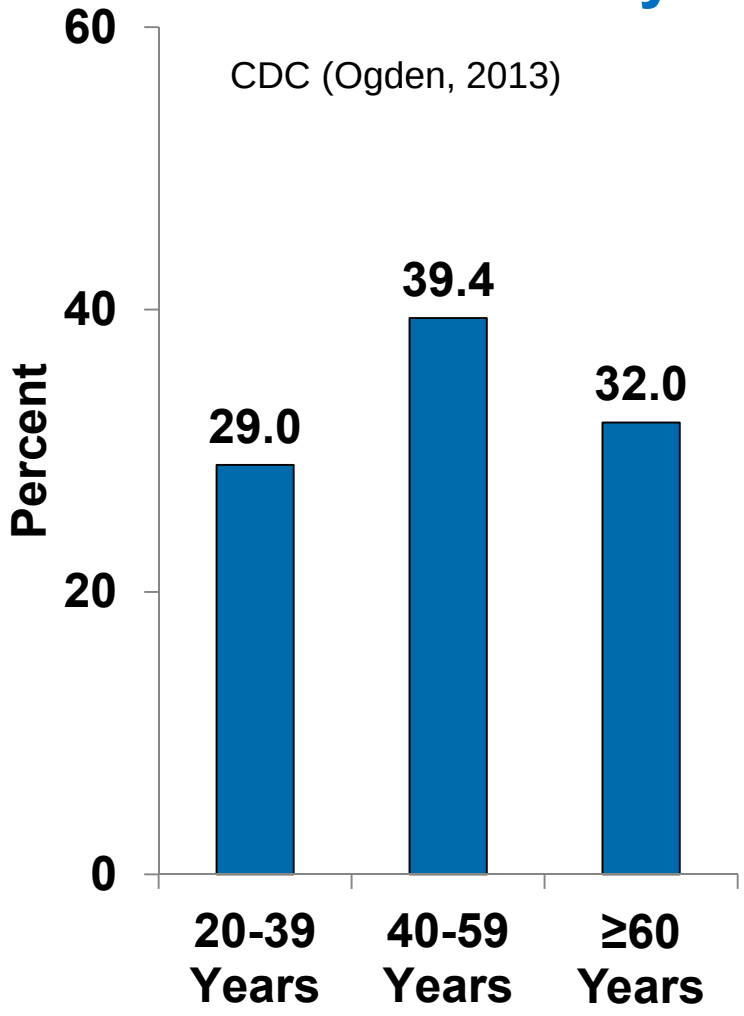
Nguyen et al N Eng J Med 2015

Prevalence of Overweight and Obesity

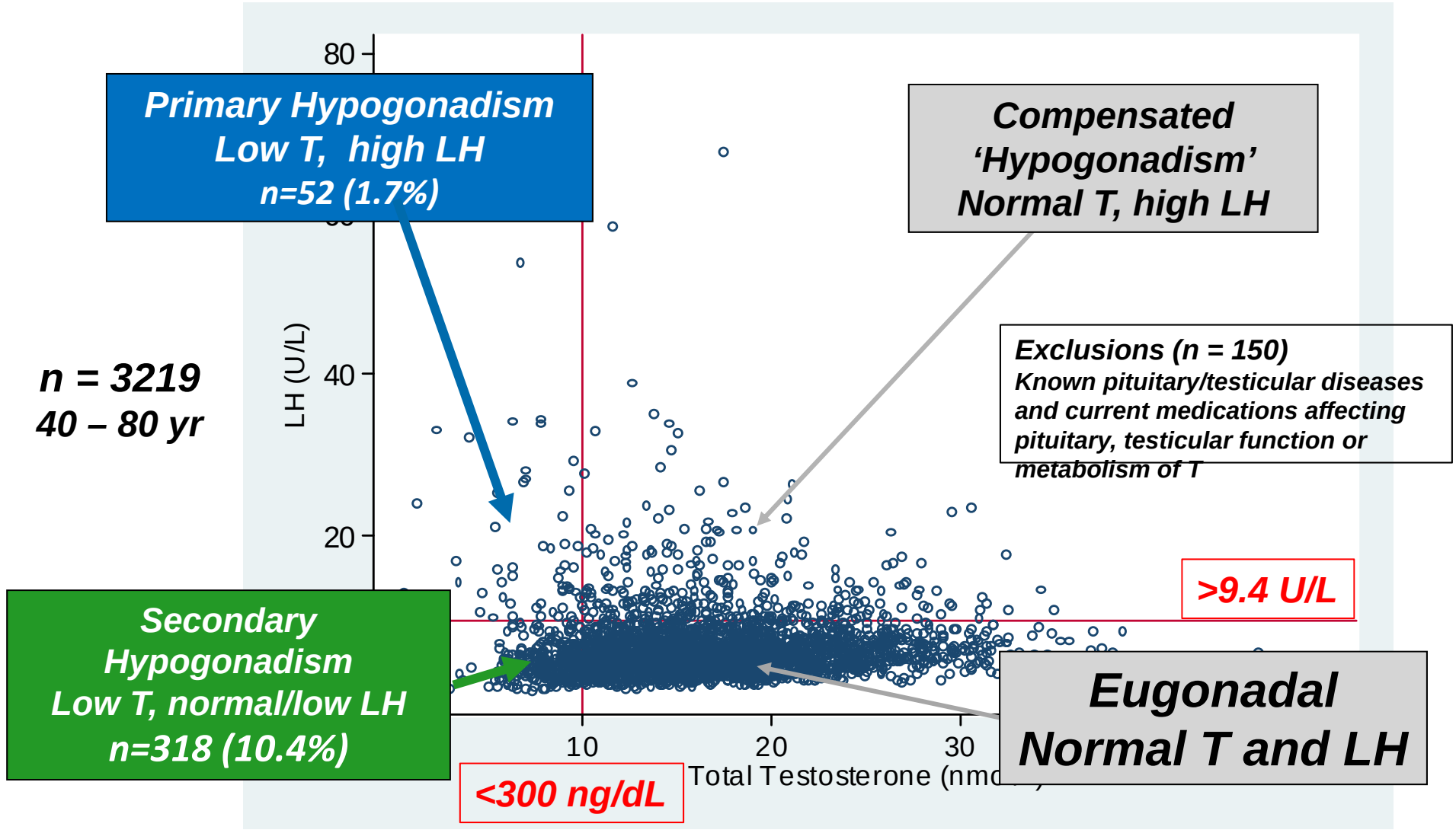
Overweight and Obese



Obese Only

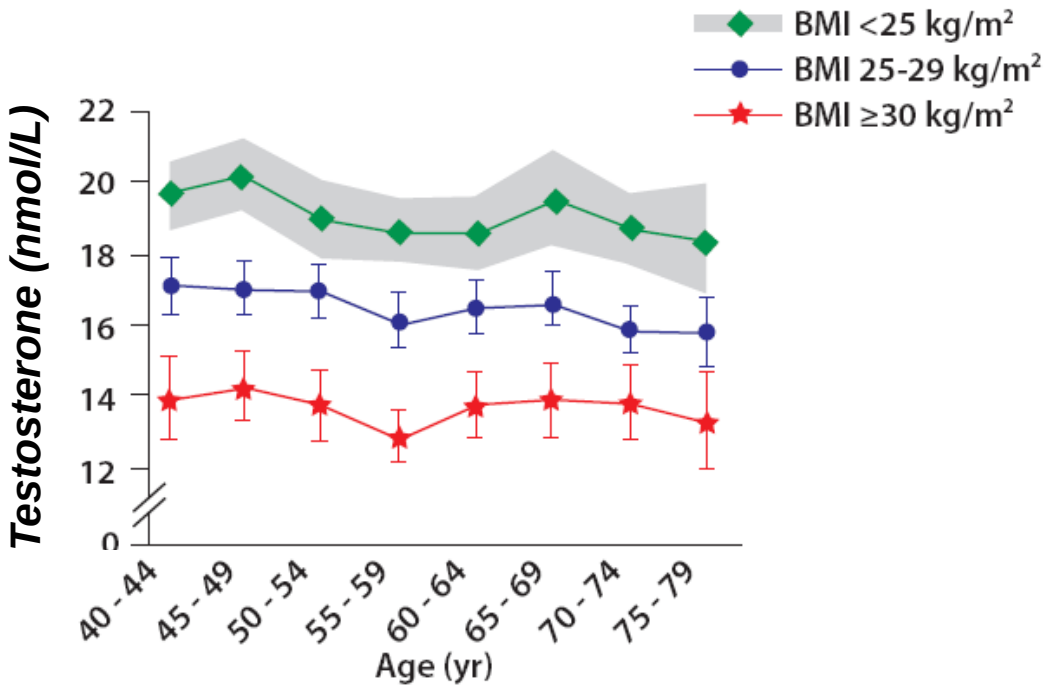


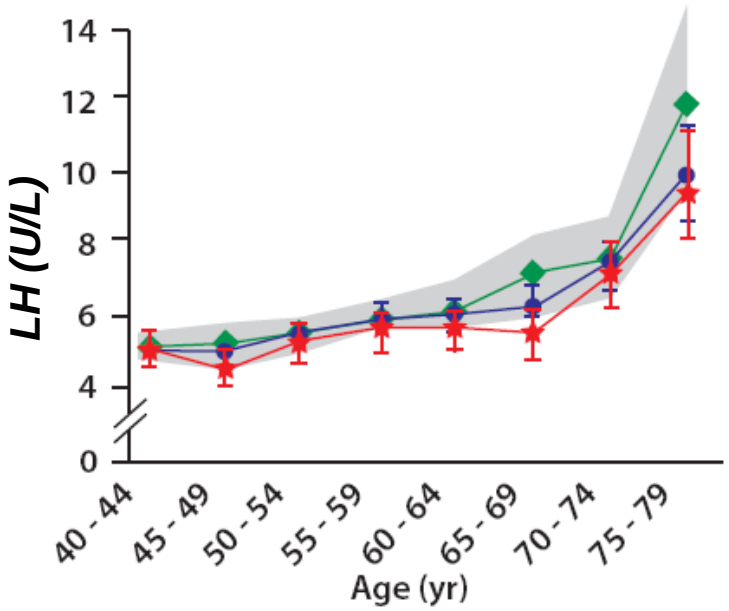
Categorizing Gonadal Status by Testosterone and LH



EMAS Tajar, JCEM 2010

BMI and Age: Different Effects on Hormones





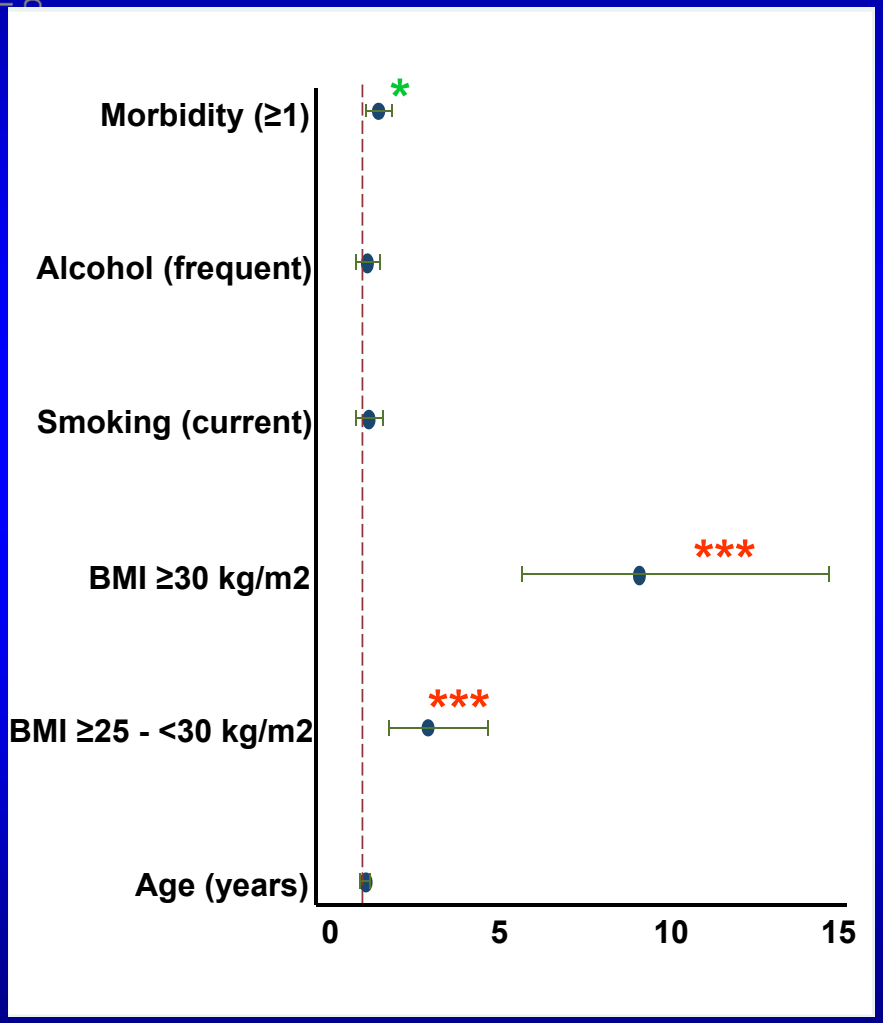
- ***With <u>obesity,</u> LH does not respond to fall in testosterone – functional hypothalamic / pituitary suppression***
- ***With <u>aging</u>, increasing LH compensates for failing testicular function so that any age-related decline of testosterone is minimized***

EMAS Wu, JCEM 2008

Secondary Hypogonadism at Baseline

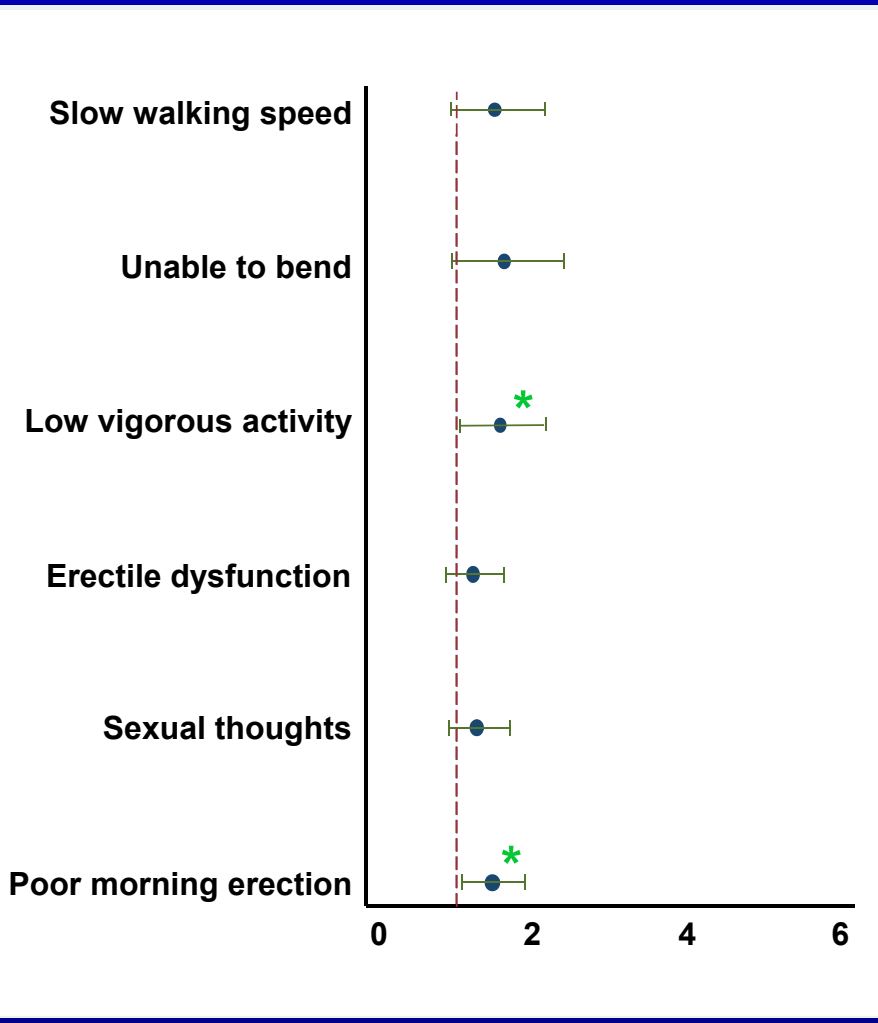
Risk factors

*p <0.05 **p<0.01 ***p<0.001



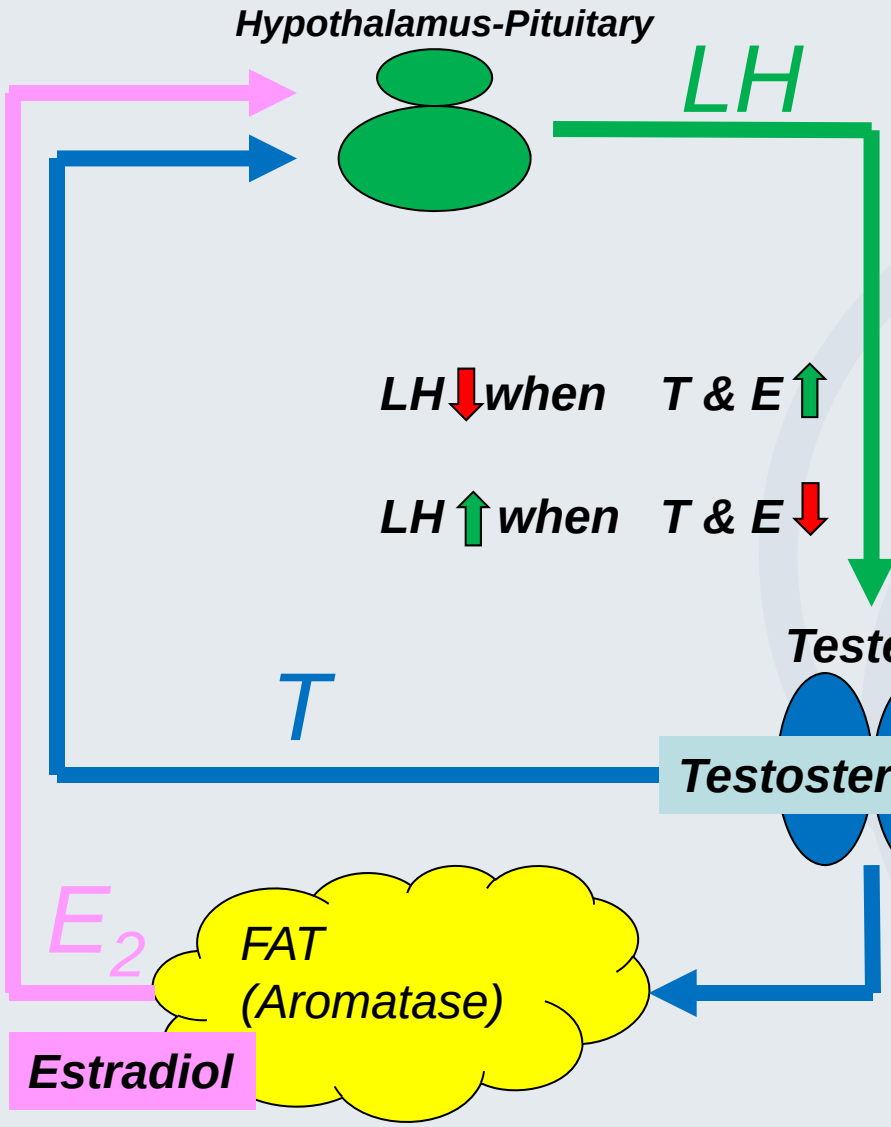
Adjusted Relative Risk Ratio

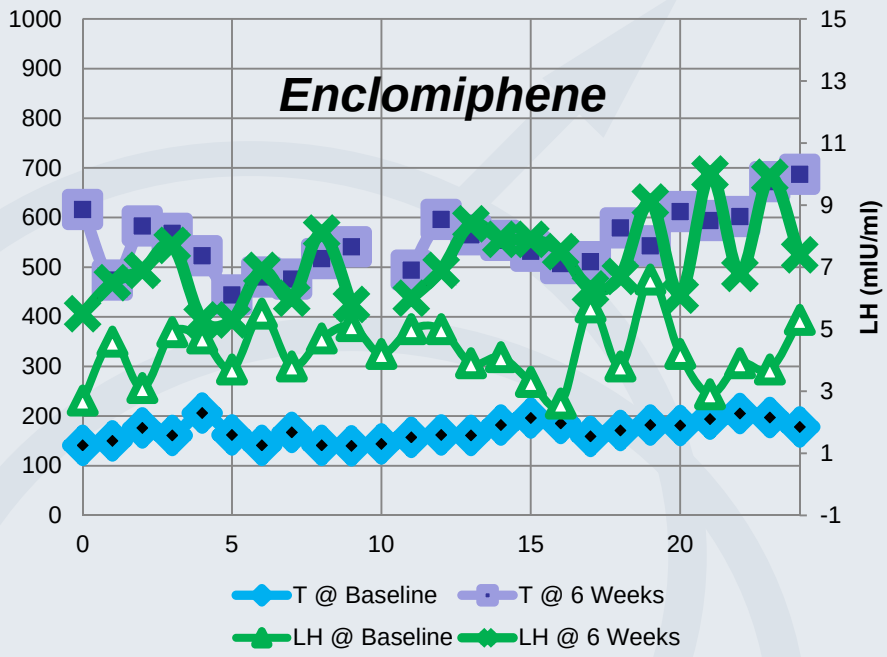
Symptoms

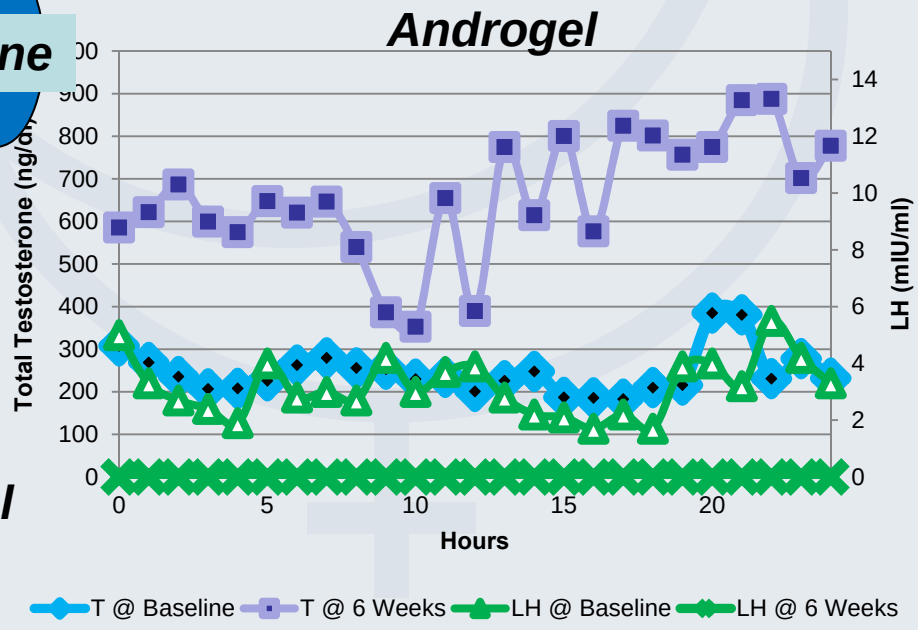


Adjusted Odds Ratio

Tajar et al. JCEM 2010







- ***Enclomiphene blocks estradiol***
- ***T further suppresses the axis***

Phase 2 Proof of Concept "Diet & Exercise" Study in Obese Hypogonadal Men - Baseline Findings

Screen 98 to enroll 50 15 Month Study

- Enrollment (n=50 in 5 weeks @ 5 sites)
- Demographics (stdev)
  - Age: 43.3 (9.2)
  - BMI: 36.8 (3.2)
  - Waist: 46.9" (4.1)
  - % Body Fat: 38.1 (5.2)
- Hormonal Status
  - Testosterone: 221.9 (52.7) ng/dL
  - Estradiol: 48.1 (14.8) pg/mL
  - T:E Ratio: 4.95 (1.7) *normal 20-25*

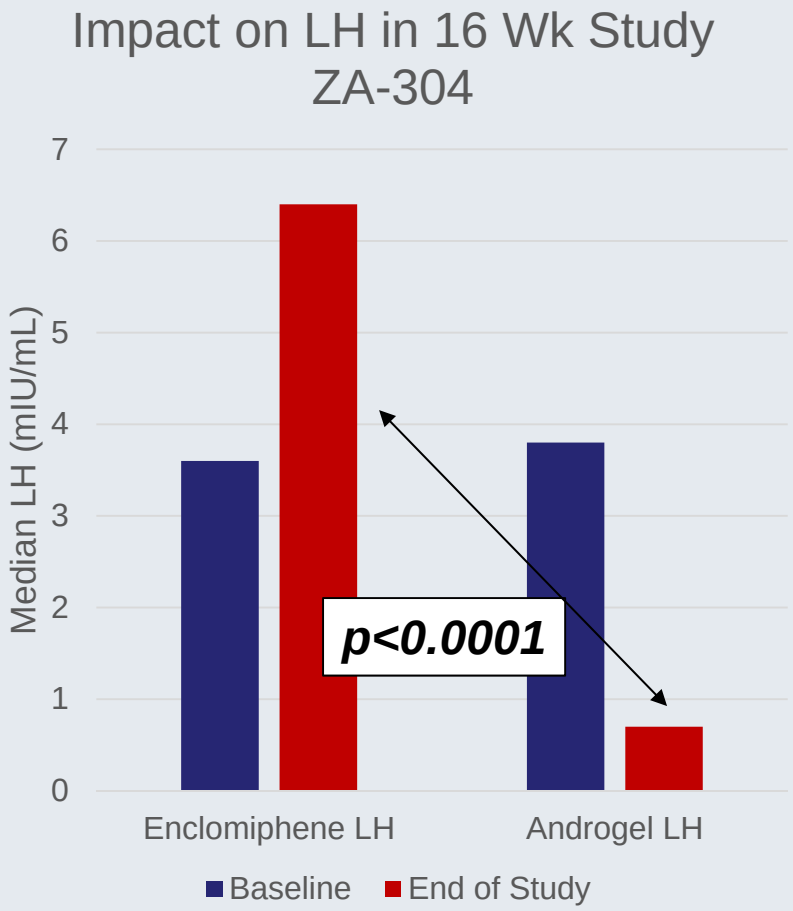
- Top 4 Reported Baseline Symptoms (% of Enrollees)
  - Fatigue/Lack of Energy: 96%
  - Depression, Irritability Lack of Focus: 74%
  - Poor Libido: 60%
  - Muscle Weakness: 48%

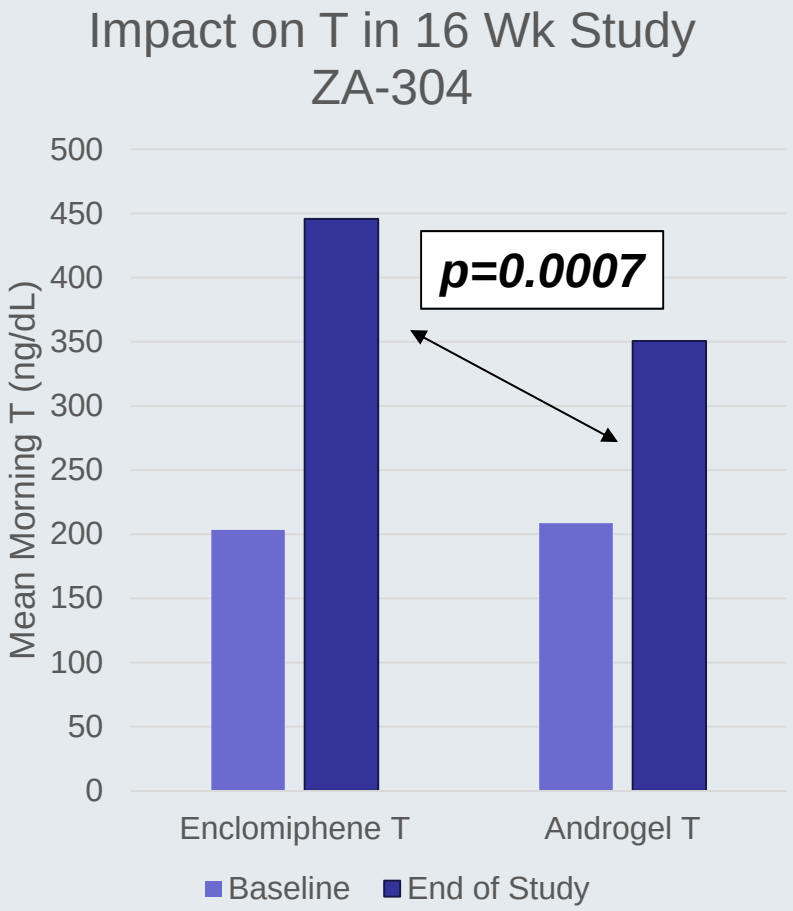
Seeks to show:

- ***The disorder is reversible with weight loss***
- ***Raising endogenous T provides benefit while attempting to diet and exercise***

How Enclomiphene Works

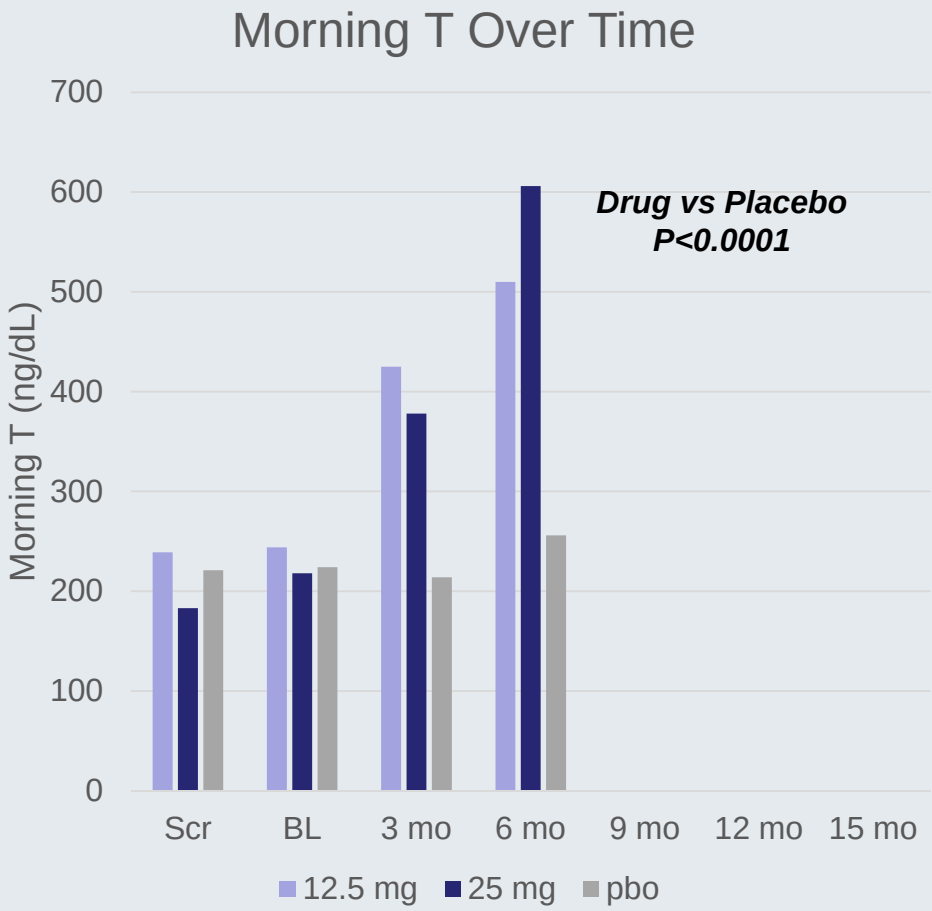
Enclomiphene *blocks estrogen at the level of the H-P axis increasing LH levels which in turn increases endogenous production of T*





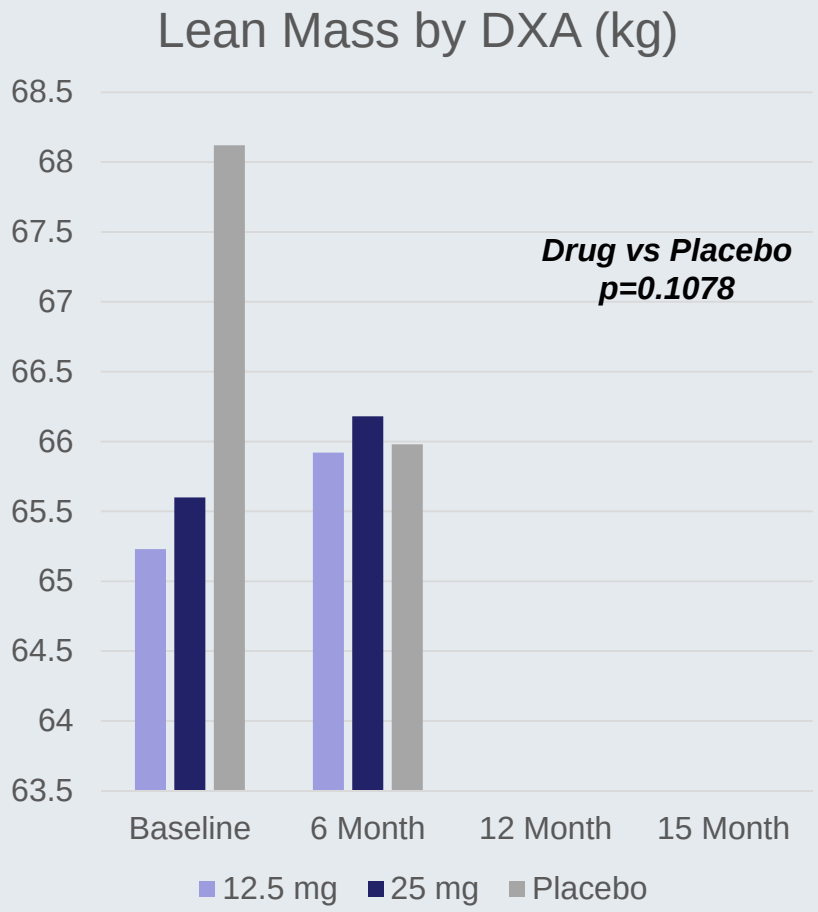
Induction of infertility and shrinking testicles in Androgel arm

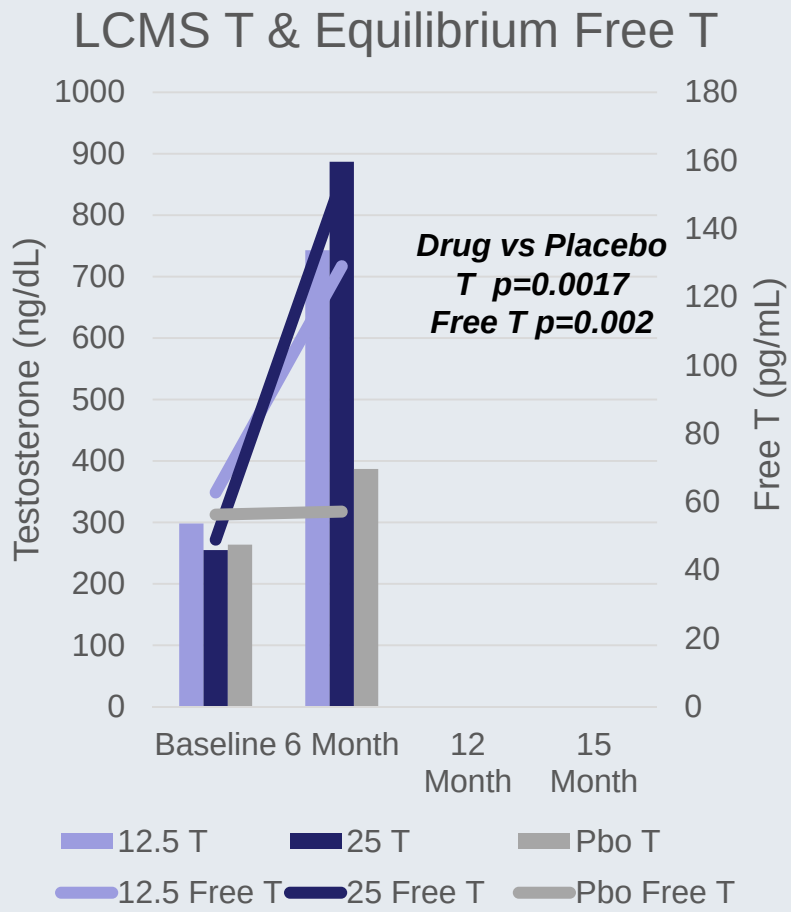
Interim 6 Month Data (CLEIA assay)
ZA-205



Commercial diet ends at 6 months.
Personal trainer ends at 12 months.

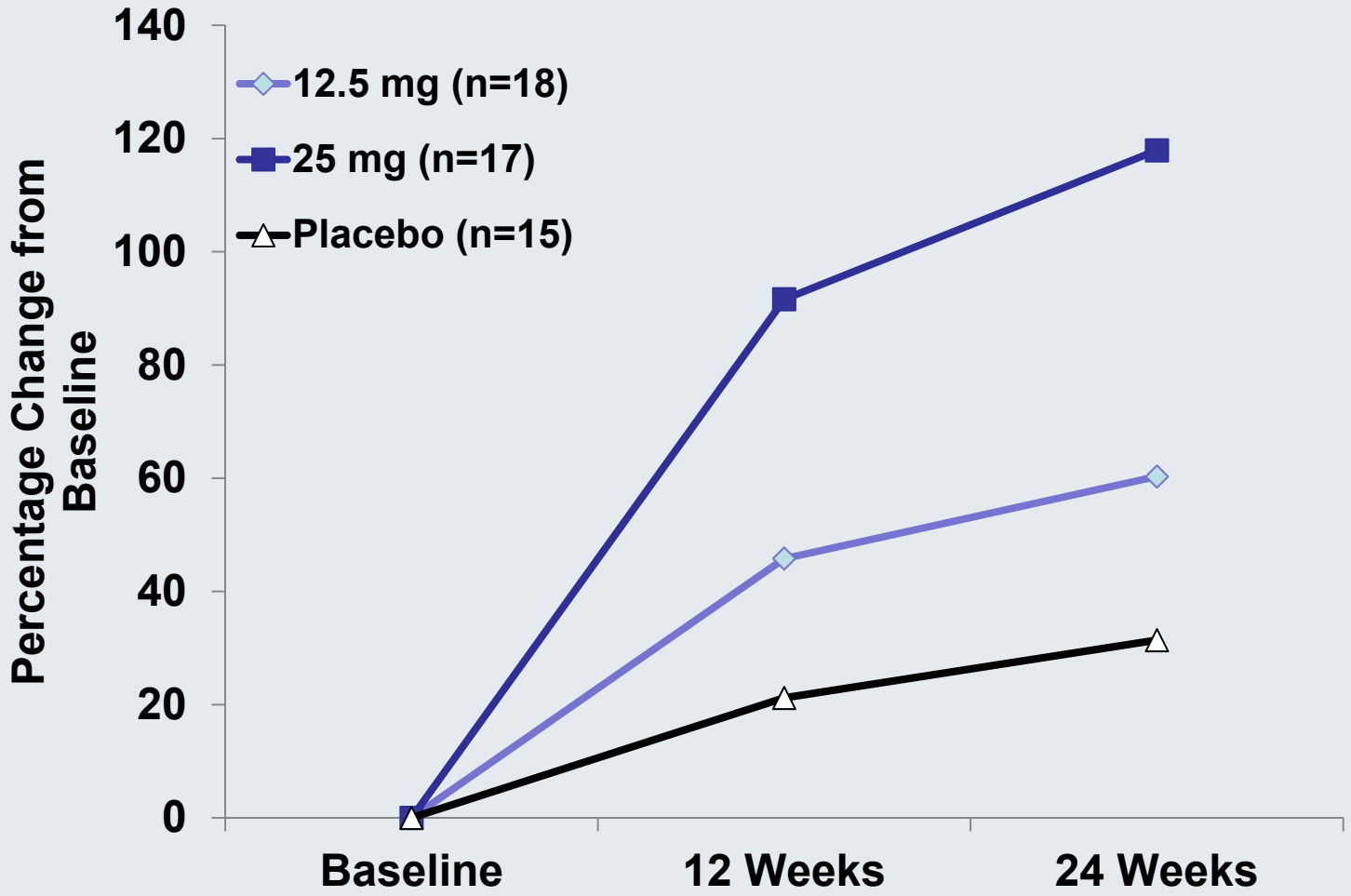
Interim 6 Month Data
Lean Mass, LCMS T & Free T





Enclomiphene arms gaining lean mass
Placebo arm losing lean mass

Ongoing Development of a Prototype PRO (early ZA-205 findings)



Relevant domains from the DISF-SR, IWQOL & SF-36
All stat sig. vs baseline

Size of Overweight and Obese US Population

It is more than a sex issue

83,740,000 Males Age 20-60

58,620,000 Overweight or Obese

28,470,000 Metabolic Syndrome

1,700,000 Symptomatic (libido, etc.) Overweight or Obese

Estimates based on CDC, EMAS and Sponsor Data

Repros Late Stage Assets

Repros seeking regional or global development/commercialization partners

Financial Summary

- **Cash and equivalents:** (unaudited June 30, 2016) $12.5 M
- **Cash used in 2016 through June 30, 2016:** $8.9 M
- **Cash runway:** Q1 2017
- **Current shares outstanding:** 24.3 M shares

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