Innovative Nuclear Receptor Modulation Medicine

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Corporate Mission

Iaterion, Inc. is Developing Novel Pharmaceutical Nuclear Receptor Co-Ligands Selective Modulators.

- Nuclear Receptors modulate the physiological effect of many critical hormones such as estrogen, corticosteroids, testosterone, thyroid and progesterone
- Changes in hormone levels throughout life results in many diseases
- Using the natural hormone (ligand) results in many positive clinical outcomes
- Yet, using the natural hormones results in many serious toxicities
- Iaterion will exploit its novel discoveries of nuclear receptor co-ligand selective modulators for unmet medical needs
First Case: Women’s Health, Menopause & Estrogen Receptor Modulators
Menopause is associated with short term and long term medical conditions

Average age of Menopause: 51 years

Average Life Expectancy of Females: 80.4 years

Average length of menopause (About 30 years)

- **Short Term Early Medical Conditions**
  - Hot Flashes: 66%
  - Sleep Disturbance: 65%
  - Mood Swings: 64%
  - Night Sweats: 55%

- **Long Term Chronic Medical Conditions**
  - Osteoporosis & Fractures
  - Cardiovascular disease
  - Early dementia & Alzheimer’s disease
  - Weight gain & Obesity
  - Type 2 Diabetes
Menopause Market Opportunity

• 55 million women are postmenopausal in US
• 5,000 women become menopausal each day in the US
• 500 million postmenopausal women in the world now and will soar to 1.1 billion by 2025
Following the WHI results, FDA added 6 “black Box” warnings to MHT, and allows MHT for short term use ONLY.
Post WHI: Change in Landscape of Menopausal Treatment

- From 2001 to 2009, total reported menopausal hormone therapy (MHT) use decreased by 52%, from 17.5 million reported use to 8.3 million
- Recent study shows that only 4.7% of women used MHT in 2010 compared to 22% in 2000

- Historically a >$10 Billion market
- Most Women’s Health conditions are not life threatening
- Therefore, therapies have to be safe
- Currently most therapies are not safe
- Specifically, unlike menopausal hormone therapies (MHT) the treatment must not result in increased risk of:
  - Breast cancer
  - Clotting events
  - Uterine cancer
  - Cardiovascular disease

Tsai. Menopause 2011 18 (4)
Menopause Commercial Potential

Total addressable market opportunity of $10.0 billion\(^{(a)}\)

Additional market opportunity from approximately 80% of menopausal women who use some form of over-the-counter (OTC) supplement to abate the symptoms of menopause\(^{(b)}\)

Branded products in this indication typically cost $4-6 / day:

Total sales of Pfizer’s Premarin family of products at generic prices of $1 / day in 2001 (pre-WHI):

Potential Market:

\[
\text{Potential Market} = \text{Total sales} \times \text{Market size} = \$5 \times 2.1 \text{ Billion} = \$10 \text{ Billion}
\]

\(^{(a)}\) Based on 2001 sales of Pfizer (Wyeth’s) Premarin family of products of 2.1 billion prescriptions. Assumes branded product cost of $5 / day

Estrogen Regulation: Evolution of the Traditional Model - One Ligand/One Receptor

A. 1900 discovery of the hormone chemical structure

B. 1982 discovery of the estrogen receptor as the mediator for cellular hormone regulation

C. 1986 discovery of structural and functional domains of the receptor

D. 1996 discovery of ERβ a second estrogen receptor

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E. 1988-2004 discovery of mechanisms of obligatory steps from ligand binding to cellular effects and biological response
Selecting Efficacious & Safer Estrogens

- Tamoxifen, originally thought as an anti-estrogen, was approved by the FDA for the treatment of metastatic breast cancer in 1977, prior to the discovery of the estrogen receptor (originally developed as “the day after pill”)
- Following the discovery of the ER, and years of clinical experience, a mixed agonist/antagonist picture emerged, when compared to estrogen
- Selective estrogen receptor modulators (SERMs) resulted in mixed efficacy and safety profiles

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<th>THE IDEAL MHT:</th>
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Potential Future Selective Estrogens for Menopause Hormone Therapy

- Long term MHT results in increased cancer risk
- SERMs utility is limited to breast cancer & osteoporosis
- SERMs cause severe menopausal hot flashes
- ERα Co-ligand reprograms estrogens effect for safe long term use
The Difference Between Co-Ligand and SERM

**Desired Clinical Effects**
- Breast cancer
- Uterine cancer
- Hot Flashes

**Adverse Effects**
- Clotting
- Obesity & Type 2 Diabetes

**SERM**
- Only SERM binds to the receptor
- Estrogen is blocked
- Mixed agonist/antagonist
- Transcription
- Reprogramed

**Co-Ligand**
- Both ligands bind to the receptor
- Transcription
- Reprogramed

**Desired Clinical Effects**
- Breast cancer, vaginal atrophy
- Osteoporosis

**Adverse Effects**
- Breast cancer
- Uterine cancer
- Clotting
- Hot Flashes
Currently Approved MHT Regimens

**Indications:** Hot Flashes and Vaginal Symptoms ONLY

**Length of Treatment:** Approved for Short term (< 5 years) due to safety
Iaterion’s MHT Regimen

**INDICATIONS:**
- Short-term symptoms - Hot Flashes and Vaginal Symptoms
- Long-term symptoms - Osteoporosis, Type 2 diabetes, Obesity

**LENGTH of TREATMENT:** Long-term (> 30 years)

*Iaterion’s Co-ligands will broaden the clinical indications of MHT and greatly expand the length of treatment*
ERα Co-ligand- Novel Discovery

A. CC7 binds concurrently with E2 but at a different site in ERα than E2
B. CC7 + Estradiol regulate 824 unique genes
C. The total number of genes regulated by CC7 + Estradiol 1358 compared to 756 with Estradiol. CC7 alone regulates on 24 genes
Reprogramming Safety with ERα Co-Ligand

A. CC7 blocks the E2 stimulation of proliferation of MCF-7 breast cancer cells
B. CC7 blocks the E2 activation of the oncogene c-Myc in MCF-7 breast cancer cells
C. Unlike Estradiol, CC7 + Estradiol does NOT cause proliferation
Potential Indications for Future ERα Co-Ligand Reprogramming Agents + Estrogens

- ERα Co-Ligand Reprogramming Agents:
  - Hot flashes & night sweats
  - Urogenital atrophy and vaginal dryness
  - Breast & Colon cancer prevention
  - Obesity
  - Metabolic syndrome
  - Diabetes & Obesity
  - Cancer prevention
  - Osteoporosis
Potential Indications for Future Nuclear Receptors

• Androgen Receptor
  – Prevention of frailty in elderly men
  – Muscle building in older men
  – Enhancement of male and female libido

• Glucocorticoid Receptor
  – Chronic pain
  – Osteoarthritis
  – Rheumatoid arthritis
Iaterion Team

- Isaac Cohen, OMD, PhD, Chairman and CEO, Over 15 years of pharmaceutical company management experience. Managed start-up to public markets enterprise. Raised over $120M in bio-pharmaceutical funding. Experience in manufacturing facilities planning, design and construction for unique biological products. Extensive experience in building scientific, engineering, regulatory and financial teams. Experience in the whole Pharmaceutical-Biotech value creation process. Holds multiple pharmaceutical patents and authored numerous scientific papers.

- Dale Leitman, MD, PhD, Chief Scientific Officer, is a Professor at the University of California, Berkeley. He is trained as a molecular biologist, physiologist and obstetrics and gynecology. Dr. Leitman is an expert in women’s health and endocrinology. He completed his training with Ferid Murad, MD, Nobel Laureate. Dr. Leitman has been consulting to the pharmaceutical industry on multiple drug development projects since 1998.

- Richard Stokvis, MD, Chief Commercial Officer, Senior International Life-Sciences Executive, trained MD, experience in Pharma Business management, product launches, product development, business development, licensing and M&A. Understands the essentials of how to construct the key building blocks of life-sciences deals and realize significant value. Market focused, with experience in teams of small Life Science Companies, Service Providers, large Multinational Pharmaceutical, Medical Technology Companies and Financial Investors. Successfully managed large project teams with different disciplines in Big Pharma and Start-ups, including Merck and Novartis.

- George Butler, PhD, Consulting Chief Regulatory Officer, Dr. Butler was formerly the vice president, Customer Relationships, Global Development of AstraZeneca, plc, a global pharmaceutical company. Prior to this, he was Vice President, head of regulatory affairs. Prior to his time at AstraZeneca, Dr. Butler was vice president and head of regulatory affairs with Novartis AG. Dr. Butler has over 30 years of healthcare research and business experience, primarily in a development environment in multiple biopharmaceutical companies and has also been active for many years in advancing Asian-Western development/regulatory single programs.

- Uwe Christians, MD, PhD, Head of Chemistry, is a Professor at the University of Colorado Health Science Center and an expert in therapeutic drug monitoring, clinical pharmacokinetics, drug metabolism, drug transport, drug interactions and mechanisms of toxicity. Dr. Christians specializes in the biodisposition of drugs and their efficacious and toxic metabolites at the cellular level, in isolated organs and in healthy volunteers and patients, so as to correlate the pharmacokinetics and pharmacodynamics for drugs in various patient populations. Dr. Christians consults for all major and biotech companies.
Drug Development - Cost & Timeline

- We will advance CC7 like drug initially:
  - ERα co-ligand for long term prevention of menopausal conditions
- Products will enter Phase 1 clinical trials in 18 months
- Initial products optimization requires $1M
- Entry into Phase 1 clinical testing will require $5
- Total cost of drug development depends on final regulatory requirements (clinical trial size, duration & procedures)
- Company will seek exit through sale/licensing of its products &/or IPO
Summary

• Iaterion discovered and developed new platform for nuclear receptor modulators & identified lead compounds

• Iaterion has knowledge, experience and capabilities to support all aspects of drug development

• Iaterion will aggressively seek global IP protection for its products (Engaged with WSGR)

• Iaterion products are designed to address large unmet medical needs with known markets