REINVENT MEDICINE FOR A HEALTHIER WORLD
Weekly Oral Levomethadone for Opioid Use Disorder

March 2022
Richard Scranton MD MPH
Disclosures and Acknowledgements

Richard Scranton MD MPH is the Chief Medical Officer of Lyndra Therapeutics

Research supported by the National Institute on Drug Abuse through the NIH HEAL Initiative under Award numbers 5UG3DA047709 and 1UG3DA050310
Long-Acting Weekly Oral Therapy for Treatment of Opioid Use Disorder
LYN-014 Weekly Oral Levomethadone

**Novel Oral Drug Delivery**
- Once weekly oral administration
- 24/7 therapeutic drug levels
- Narrower range of plasma concentrations

**Patient Centric**
- Ease of use
- Reduced stigma
- Potential for improved safety profile

**Reshaping Methadone Maintenance Therapy**
- Levomethadone is more potent and potentially safer than methadone
- Access opportunity
- Patient empowerment
- Remote monitoring
Multiple scientific discoveries and engineering innovations underlie Lyndra’s success in long-acting oral drug delivery

- **Elastomeric core**
  - Designed to withstand thousands of contractions

- **Disintegrating matrices**
  - Formulated to enable tuned disassembly of stellate

- **Active arm matrix**
  - Enables controlled drug release from the underlying polymer matrix

- **Active arm coating**
  - Linearizes drug release over the course of weeks

- **Capsule coating**
  - Functional coating that ensures precise deployment in the stomach

- **Dosage Form encapsulation**
  - Methods that enable folding and placement of stellate into capsule

**More than 300 drug administrations**
- 4 IND approved with active studies ongoing across various disease states including schizophrenia, cardiovascular, diabetes
- Robust preclinical program and chronic toxicity studies demonstrating safety
Drug Arms: Controlled Drug Delivery

2020 Schizophrenia Phase 1 study

LYNX™ platform technology has progressed rapidly through proof of concept to clinical studies in 4 therapeutic areas.
The LYNX™ platform uses a preferred oral form with an innovative delivery system.

Nearly 90% of patients and caregivers surveyed say they prefer pills...

...and 80% say they find the concept of a weekly pill appealing.

Source: HawkPartners Patient Unmet Needs Survey (Q3’21; n=1645 patients and caregivers)
The CDC estimates there were 75,673 overdose deaths in the US attributable to opioids in the 12-month period ending in April 2021, the highest level ever.
Weekly Levomethadone for Opioid Use Disorder: granted Fast Track Designation

**LINEAR IN VITRO RELEASE**

- Full FaSSGF Release (%)
- Full FaSSIF Release (%)
- 1 day Switch Release (%)
- 3 day Switch Release (%)
- 5 day Switch Release (%)

**DOG PK SHOWS CONSISTENT RELEASE OVER 7 DAYS**

- LYN-014-M + fluconazole
- LYN-014-M
- IR methadone

Consistent reproducible drug release over 7 days with various simulated gastric conditions.

Preclinical data demonstrates a once weekly levomethadone is possible.

Note: Methadone is rapidly metabolized therefore, a standard protocol of co-administered fluconazole permits quantification of drug levels.
Predicted Human PK Profiles of Levomethadone after IR followed by LYN-014

- Physiological based pharmacokinetic (PBPK) models have been developed to predict exposure of levomethadone after LYN-014

  - The predicted $C_{\text{max}}$ after 280 mg and 420 mg LYN-014 weekly was lower than the exposure at maximum recommended methadone dose (120 mg methadone or 60 mg levomethadone).
  
  - Phase 1 study intended to provide low dose of levomethadone to confirm safety threshold
Digital monitoring technologies will provide valuable insights into future remote monitoring capabilities
1. Intelli-Heart ROCT, Real-Time Outpatient Cardiac Telemetry, continuous monitoring

2. Masimo SafetyNet, oxygen saturation and pulse, continuous monitoring

3. Continuous oxygen saturation and pulse monitoring with alerts, participant safety
LYN-014 and Digital Health Technology

The Helping to End Addiction Long-term® Initiative, or NIH HEAL Initiative®, is an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis.

A look at the future of LYN-014 dosing:
- Determine fit-for-purpose technology
- Advance meaningful innovation
- Support tech equity (techquity)
- Promote patient centricity (patientricity)

---

**LYN-014 Current Inpatient Model**
- Participant safety and Investigator trust key selection factors
- First wearables for Lyndra with future gaze
- Study coordinators to set up and maintain mobile health tech 24/7
- Participant burden as essential issue

**LYN-014 Hybrid Study Model**
- Expand new mHealth tech to support outpatient days and visits
- Include innovations for later safe dosing in the community
- Provide participant cell phones as needed and 24/7 IT support
- Participant choice for remote or in person study visits

**LYN-014 Remote Treatment Model**
- mHealth tech to promote a meaningful patient feedback loop
- Include activity tracking for real time relapse correlation data
- Holistic tech provision and support bridging the digital divide
- Becomes a framework for community based, patient centric OUD recovery

---

- Healthcare Leaders Join Forces to Transform Digital Clinical Trials Through Diversity, Equity and Inclusion [prnewswire.com]
- DH Action PI [fda.gov]
- duke-margolis_mhealth_action_plan.pdf
Synergies of Once Weekly Oral Administration and Benefits of OUD Therapy
Weekly Levomethadone for Opioid Use Disorder: A Novel Solution That Addresses Many Current Challenges

**CURRENT CHALLENGES**

**Limited access to treatment**
- Not enough HCPs to treat the 2.7M people with OUD
  - Only ~ 7% of physicians are trained to treat OUD
- Only ~ 11% of people with OUD receive specialty treatment
- Clinics are often difficult to access

**Logistical and Social Barriers**
- Clinics only in certain locations, mostly large urban areas
  - Especially challenging for those living in rural or remote settings
- Few clinics offer take-home medication options because paperwork intensive for HCPs
- Risk of diversion
- Stigma associated with OTP

**FUTURE OPPORTUNITIES**

**Legislation passes to support increased use of take-home treatment**, including:
- Increased use of telemedicine
- Allowing alternate sites of care (e.g., pharmacy)

**Introduce oral weekly treatment to:**
- Improve patient adherence to treatment
- Reduce risk of diversion due to weekly vs. daily administration

**Reduced stigma and improved recovery experience**

Transforming OUD Treatment Paradigm will Require Multipronged Approach
Since March 2020, the US Substance Abuse and Mental Health Services Administration (SAMHSA) allowed for an increase in methadone take-home doses for the treatment of Opioid Use Disorder (OUD)\(^2\)

- Extended in November 2021 for 1 year\(^3\)
- Congress has introduced new legislation (Opioid Treatment Access Act, 2022) to improve access to treatment for opioid use disorder (OUD)\(^4\)
  - Building on COVID-19 exemptions that allow more flexibility for take-home doses
  - Allow pharmacies to dispense methadone to OTP patients
  - Conduct full study on impact of take-home treatment
  - Codifying regulations that allow OTPs to operate mobile without separate DEA registrations

Studies show improvement in treatment access with reduction in hospitalizations from the relaxation of treatment guidelines for OUD\(^1\)

- Pre COVID-19 Exemption: 74, Post COVID-19 Exemption: 56

- A convenience sampling study of 249 patients\(^1\) during the pandemic showed an increase in mean take-home doses by 200%
- This increase in flexibility was not found to be associated with poorer treatment outcomes, while increasing patient satisfaction

COVID-19 has reshaped the treatment paradigm for opioid use disorder allowing for the relaxation of methadone take-home protocols

Once Weekly Long-Acting Oral OUD Therapy

- With the impact of COVID-19, the increase in adoption in a remote care delivery model has benefitted patients with lower barriers to receive care while increasing adherence on medications
- SAMHSA’s new policy of take-home protocols for OUD has allowed an increase in access to treatment options for patients
- New legislation to allow OUD treatment dispensing at pharmacies could greatly improve access and reduce stigma
- Near-patient, remote, or mobile care facilities could remove barriers in socio-economic determinants for treatment

Telemedicine / Virtual Treatment Programs

- Pharmacy dispensing
- Mobile OUD treatment
- Traditional clinic visits
- Better patient outcomes
- Improved adherence
- Reduction of overdose & abuse

Improved Patient Satisfaction/Reduced Stigma

Through our support from NIH/NIDA: Lyndra is committed to combating the opioid epidemic by rapidly progressing a once-weekly Levomethadone therapy to treat Opioid Use Disorder
NIH HEAL Initiative and Helping to End Addiction Long-term are service marks of the U.S. Department of Health and Human Services.

Thank you.