Enalare Therapeutics Inc.

Developing Novel Therapies for Life-threatening Critical Care Conditions

January 2022

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Driving Strong Momentum Towards Vision of Creating Global Blockbuster Critical Care Products

Company Profile

- Portfolio of First-in-class New Chemical Entities (NCEs) with strong IP into the 2040s
- Multiple products with potential to address significant unmet medical needs in the community, hospital, and battlefield settings
- Commercial blockbuster potential across Post Operative Respiratory Depression, Drug Overdose, Apnea of Prematurity, and other serious conditions
- Strong leadership with world class scientists and top tier industry operators

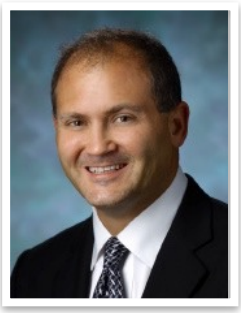
Recent Milestones

- Executing breakthrough clinical study as the first product to reverse the respiratory depressive effects of propofol – important study supporting several pipeline products
- Developed new intra-muscular (IM) formulation in partnership with BARDA to use as Medical Countermeasure for potential mass casualty events and community drug overdose
- Filed new patents expected to extend worldwide exclusivity to 2042
- Received Rare Pediatric Disease designation by FDA for Apnea of Prematurity indication

Enalare is Led by Top-tier Industry Operators with Clear Focus on Execution and Building Enterprise Value

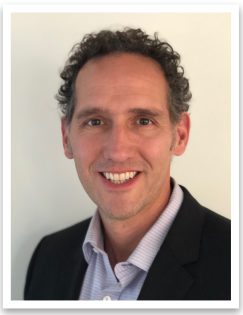
Herm Cukier
Chief Executive Officer
& Board Member

- CEO and Board Member of BioDelivery Sciences (NASDAQ: BDSI)
- SVP of Allergan - leading several multi-billion dollar divisions
- Chief Marketing Officer and Member Company Management Team - Organon Biosciences
- Executive positions with top tier companies including Bayer, BMS, and Pfizer
- MBA Columbia Business School
- BSE University of Pennsylvania



Dr. Joseph Pergolizzi
Chief R&D Officer
& Board Member

- Internationally recognized thought leader in areas of perioperative and pain medicines, drug development and regulatory affairs
- Highly published in top tier journals
- Frequent scientific advisor for public and private companies
- Serial entrepreneur, started more than 20 companies
- Johns Hopkins School of Medicine
- Georgetown School of Medicine - residency



Daniel Motto
Chief Operating Officer

- EVP Hikma Pharmaceuticals leading US Injectable Division
- SVP Allergan (Actavis) - Head of Business Development, Portfolio & Business Intelligence, Global Generic Medicines
- SVP Teva, Global Business Development
- Executive positions with top tier companies including Johnson & Johnson and Novartis
- MBA Johnson College of Business, Cornell University
- MS Engineering, Cornell

Board of Directors

Gino Santini
Former member of Eli Lilly's executive committee leading Corporate Strategy and Business Development. Prior roles over a career spanning nearly three decades included president of US operations, various leadership positions in international regions and president of the women's health franchise. Board member of multiple public companies including Horizon, Collegium and Intercept Pharmaceuticals.

Bob Yedid
30 yrs of experience as a buy-side analyst, portfolio manager, private equity investor and investment banker holding positions at Warburg Pincus and Bear Sterns. Currently focuses on providing CEOs and CFOs with strategic advice on key investor issues at LifeSci Advisors. Former Board member of The Medicines Co. and Vaxart. MBA Stanford School of Busines, BA Yale University.

Joseph Petko
20 yrs experience in corporate finance and investment analysis. Currently co-Chief Investment Officer for public equity investing at Ashford Capital, with a focus on small cap growth companies. Prior experience in financial positions in the pharmaceutical industry at Merck & Co. MBA Lehigh University, BBA Wharton, University of Pennsylvania.

Mark Coleman, MD
President of National Spine and Pain Centers, the nation's largest interventional pain management group. Early advisor in the formation of Axsome Therapeutics and a member of its board of directors since 2014. Diplomat of the American Board of Anesthesiology and highly sought after pharmaceutical and medical device scientific advisor. MD from Johns Hopkins University School of Medicine, BA Wesleyan Univ.

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Scientific Team Supported by Globally Recognized Subject Matter Experts

Scientific Advisory Board

Lead Investigator

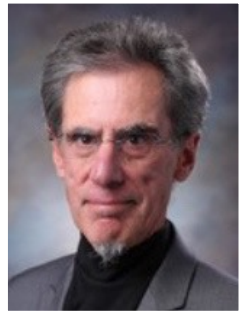
World renowned expert in areas of anesthesia and pain and advisor to top regulatory agencies. Founder and Head of the Anesthesia & Pain Research Unit at Leiden University. Member of several editorial boards and has published hundreds of articles in peer reviewed journals. Leiden University Medical Center, Professor of Anesthesiology

Albert Dahan, MD, PhD

Lead Investigator

Distinguished leader in anesthesiology working to define best-practice. Chairman of the Department of Anesthesiology at Stoney Brook Medicine and former faculty at the Duke Clinical Research Institute. Founding President of the American Society for Enhanced Recovery (ASER) and dedicated to improving perioperative care through his role in establishing Enhanced Recovery After Surgery (ERAS) programs.

TJ Gan, MD



Internationally renowned scientist and key opinion leader in pain pathways and analgesics. Over 30 years industry, academia and government experience in engineering and pharmacology. Former team co-leader for analgesics drug discovery at Johnson & Johnson. Currently affiliated with University of Arizona College of Pharmacy and Temple University School of Pharmacy

Robert Raffa, PhD

A seasoned healthcare executive with over 20 years of experience, spanning academia, industry and management consulting. Prior to establishing TrueNorth Lifesciences, David served as a senior principal in the consulting practice within IMS Health. MD, Weill Cornell Medical College, MBA Wharton School of Business, M.Sc. Harvard School of Public Health

David Battleman, MD

Accomplished international executive with over 20 years experience in the pharma industry. Former Head of Pharmaco-kinetics at Grünenthal GmbH and Vice President TRF Business at Grünenthal USA, Inc. Frequent presenter on abuse prevention of prescription drugs. Former Head of Search & Evaluation at Aquestive Therapeutics.

Alexander Kraus, PhD

Practicing emergency medicine specialist with experience treating substance abuse and COVID-19 patients at the largest provider of healthcare in NY State, Northwell Health. Serves as the Medicine Lead for both the Opiate Task Force and Sepsis Task Force. Research experience at Northwell Health, Cornell-Presbyterian Hospital, and University of Medicine and Dentistry of New Jersey

Eugene Vortsman DO

Enalare Team Highlights

Alfred Schweikert, PhD, RAC - Regulatory Affairs & Quality Assurance

Over 35 years experience in the pharmaceutical industry, with 25 years devoted to management of regulatory affairs. Extensive global regulatory and development experience with drugs, devices and biologics covering the full life-cycle of development to post marketing. Prior roles with Hoffman La Roche, Schering Plough, Johnson & Johnson, and Baxter.

Thomas Miller, PhD – Clinical Development

More than 20 years of experience in the development of biophysical and pharmacological interventions targeted primarily at critical care pulmonary function and attenuation of ventilator-induced lung injury. Has established and led clinical development globally for the introduction of disruptive medical technologies, including the creation of a new standard of care and playing a significant scientific role in the path to an IPO. Prior roles with Vixiar Medical, Vapotherm and Nemours.

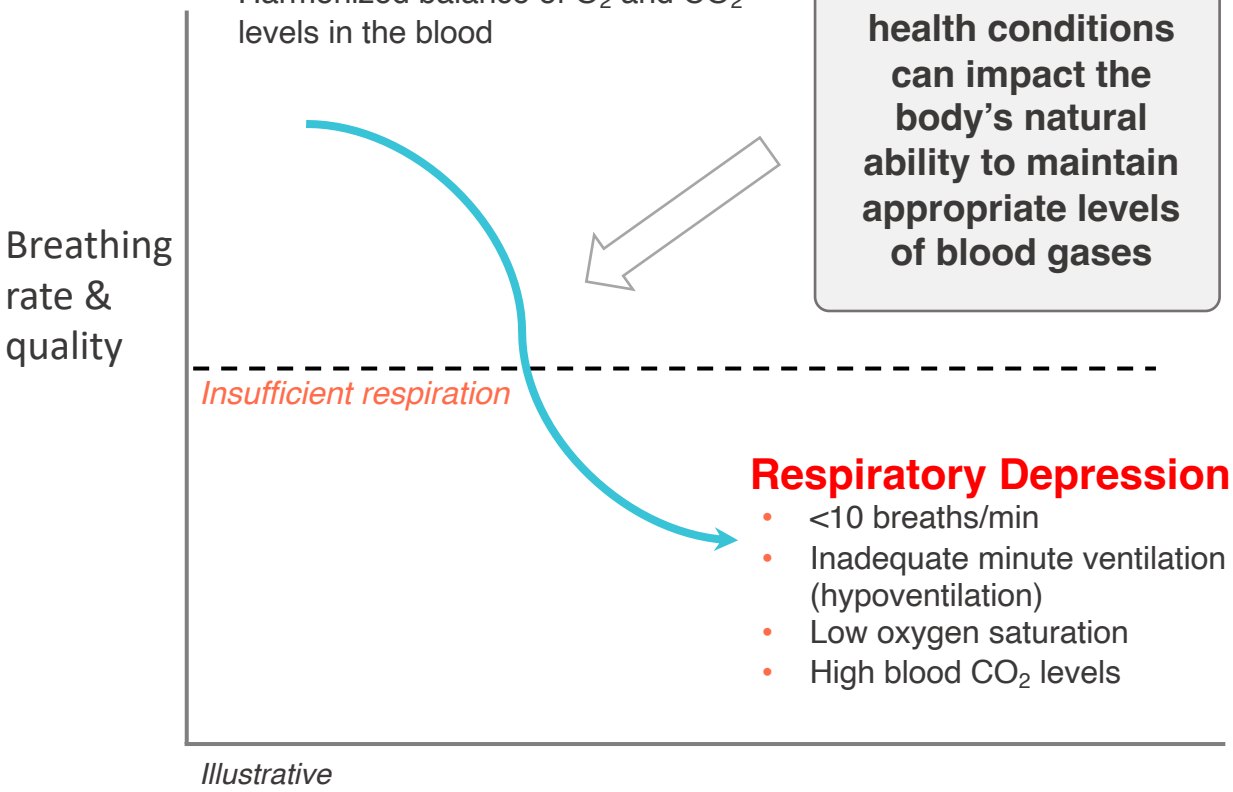
Frank Diana, PhD – CMC & Formulation Development

More than 30 years experience with CMC (Chemistry, Manufacturing and Controls), Analytical and Pharmaceutical Development for early development through NDA/BLA submission as well as for marketed products. Prior roles with Endo Pharmaceuticals, Johnson & Johnson and DuPont.

The Problem to Solve: Acute Respiratory Depression
A Global Health Emergency Endangering Millions of Patients

Normal Healthy Respiration

- 12-20 breaths/min
- Minute ventilation of 5 to 8 liter/min (resting)
- Harmonized balance of O_2 and CO_2 levels in the blood



Medications and health conditions can impact the body's natural ability to maintain appropriate levels of blood gases

Prioritized Target Markets

Post-Operative Care

- Unmet medical need, 10x in-hospital mortality risk[2]
- 70mil+ surgeries in US performed annually with large at-risk populations – age, obesity, other health conditions
- Compelling health economic benefits by reducing ICU/overall hospital length of stay

Drug Overdose

- US deaths reached record high of 93K[1] in 2020 and still increasing
- Polysubstance (multi-drug) abuse a growing issue
- Current treatment option is incomplete – only addresses opioid overdose, potential severe withdrawal symptoms

Apnea of Prematurity

- Infants born preterm are predisposed to life-threatening episodes of cessation of breathing[3]
- Current standard of treatment is caffeine – not effective for all patients
- Opportunity for Orphan Drug/Rare Pediatric Disease designations

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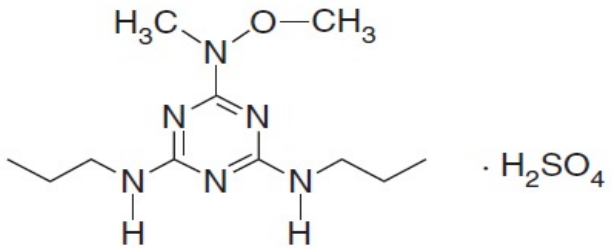
[1] US HHS, Centers for Disease Control and Prevention (CDC), Provisional Drug Overdose Death Counts 12-month ending Dec. 2020
[2] Postoperative Respiratory Failure, Thompson, Shaun L.; Lisco, Steven J, International Anesthesiology Clinics. 56(1):147-164, Winter 2018
[3] Merck Manual, Arcangela Lattari Balest, 2019, Pediatrics, Respiratory Problems in Neonates, Overview of Perinatal Respiratory Disorders

The Potential Solution: ENA-001 is a One-of-a-Kind New Chemical Entity (NCE) that Stimulates Breathing

Agnostic Respiratory Stimulant

- **Agnostic**: Novel mechanism-of-action (MoA) - inhibits Big Potassium (BK) ion channels
- **Peripheral**: Affects ventilation via the peripheral chemoreceptor pathways in the carotid body
- **Natural**: Utilizes the body's ventilation control system to beneficially influence breathing



ENA-001 hydrogen sulphate salt

2-N,O-dimethylhydroxylamino-4,6-bispropylamino-s-triazine

Differentiated Product Profile

- Rapidly stimulates ventilation in patients with acute respiratory insufficiency
- Addresses both hypercapnia (high CO_2) and hypoxemia (low O_2)
- Safe and well tolerated in humans
- No interference with pain suppression or sedation
- Avoids the withdrawal effect experienced with opioid antagonists
- Parenteral administration – infusion or intramuscular injection

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ENA-001 Shown to be Safe and Efficacious Across Multiple Human Clinical Trials Totaling >100 subjects

Study	Description	# of Subjects
GAL-021-101	Single, ascending dose study in healthy subjects.	30
GAL-021-102	Extended the dose range explored during the initial study by a factor of 2 and established the maximum respiratory stimulatory dose in the healthy subjects without concomitant use of opioids or anesthetic agents.	18
GAL-021-104	Assessed the potential therapeutic utility under conditions that simulate the post-operative state. Alfentanil was used to suppress ventilation.	23
GAL-021-106	Designed to evaluate the safety and tolerability in healthy subjects during 5 days of 12-hour continuous infusion of 0.125, 0.25, and 0.5 mg/kg.	28

NEW - On-going Clinical Study 108

ENA-001-108: Breakthrough Study with Propofol Building on Strong Foundation of Existing Human Data

- Reverse the respiratory depressive effects of propofol
- Show increased ventilatory response to hypoxemia
- Targets highly utilized surgical anesthetic
- No currently approved drug for this indication
- Interim Analysis in 1Q 2022
- Full study report 2Q 2022

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Global Exclusivity Expected into 2040s Anchored by Issued Composition-of-Matter Patents

Issued Composition-of-Matter Patents

- **US 9,351,972**

  Compounds as Respiratory Stimulants for Treatment of Breathing Control Disorders or Diseases

  Includes NCE and Pharmaceutical Composition claims

  Expires Nov. 2031 (+5 yr PTE* opportunity to 2036)

- **US 9,162,992**

  Compounds and Compositions for Treatment of Breathing Control Disorders or Diseases

  Includes NCE, Pharmaceutical Composition and Method of Treatment claims

  Expires Nov. 2031

Filed Patent Applications - Coverage into 2040s

- Pending International PCT Application directed to combination therapy for the treatment of opioid overdose, stimulant overdose and polypharmacy overdose. Anticipated expiration of 2041
- Pending U.S. Provisional Application directed to composition and methods for the treatment of respiratory depression in infected patients (including COVID-19). 2041
- Pending U.S. Provisional Application directed to the reversal of respiratory depression from non-opioid central nervous system depressants, including common surgical anesthetics. 2042
- Pending U.S. Provisional Application directed to parenteral formulations of ENA-001 and related compounds. 2042

Filing strategy in place for future patent opportunities including addition pharmaceutical formulations, pharmacokinetic/pharmacodynamic profiles, new indications and dosing regimens

*Patent term extension

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Partnership with BARDA has Accelerated Development of an Intramuscular Formulation

Medical Countermeasures.gov

BARDA Request A Meeting PHEMCE Partners

BARDA and Enalare Therapeutics announce partnership to advance ENA-001 as an emergency treatment for opioid-induced respiratory depression in the community setting

WEB ANNOUNCEMENT

SHARE

BARDA and Enalare Therapeutics have partnered to reformulate ENA-001 for use as an emergency treatment against opioid-induced respiratory depression (OIRD). Respiratory depression is a condition characterized by slow and ineffective breathing (hypoventilation) that can result in low levels of oxygen and high levels of carbon dioxide and can be life-threatening if left untreated. OIRD can occur after the use of opioid analgesics and can progress to respiratory failure.

Under the Repurposing Drugs in Response to Chemical Threats (ReDIRECT) program from BARDA's Division of Research, Innovation, and Ventures (DRIVe), BARDA will provide funding to reformulate ENA-001 for intramuscular administration and preclinical pharmacokinetic testing of the new formulation. A new chemical entity (NCE), ENA-001 is an agnostic respiratory stimulant drug that may be useful as a potential emergency treatment for OIRD and other types of respiratory depression. ENA-001 is the third repurposed candidate being supported by BARDA's ReDIRECT program. If studies are successful, reformulating ENA-001 for intramuscular administration could enable its rapid use as a medical countermeasure to treat life-threatening respiratory depression in both mass casualty situations and in everyday opioid and other drug overdoses.

Biomedical Advanced Research and Development Authority partnership

- US HHS division with mandate to protect Americans and respond to health security threats
- Partnership includes funding, scientific guidance, and active engagement with FDA interactions
- Focus on development of an intramuscular (IM) formulation for use in the community setting
- IM formulation currently being optimized within animal studies
- Opportunity for expanded relationship and additional funding in next stage of partnership

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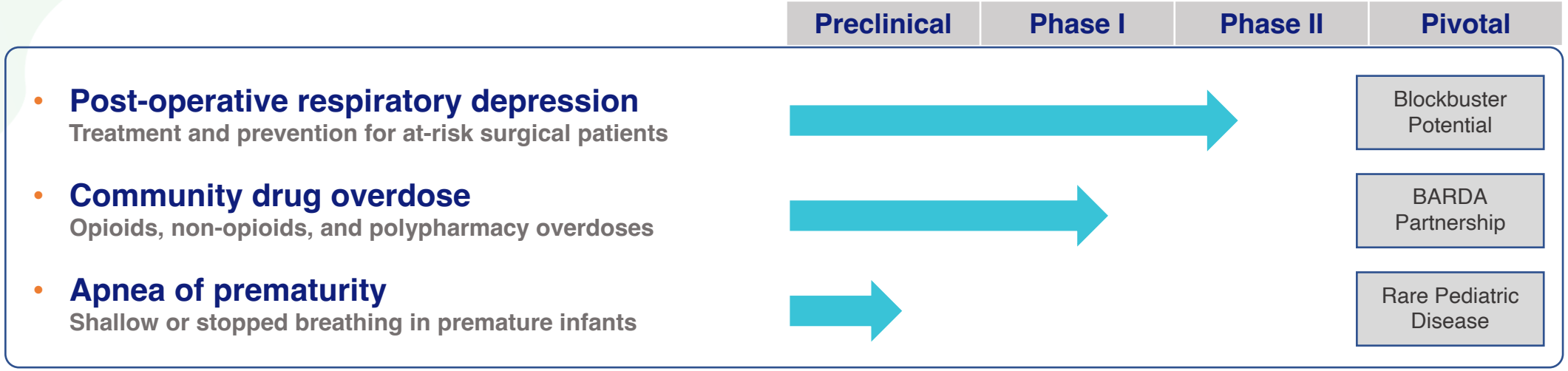
Pipeline Focus is on Initial Three Products Expected to be in Early to Mid Clinical Stage in 2022



- **Infection related silent hypoxemia (e.g. COVID-19)**
  Silent hypoxemia associated with bacterial or viral infections
- **Community drug overdose – combination product**
  ENA-001 in combination with an opioid antagonist
- **Chronic pulmonary disease with acute hypercapnia**
  Acute respiratory insufficiency superimposed on COPD
- **Sleep Apnea**
  Sleep disorder in which breathing repeatedly stops and starts
- **Altitude Sickness/Acute Mountain Sickness**
  Hypoxia and related symptoms due to ascent to high altitude

Additional product opportunities present future value creation and strategic options

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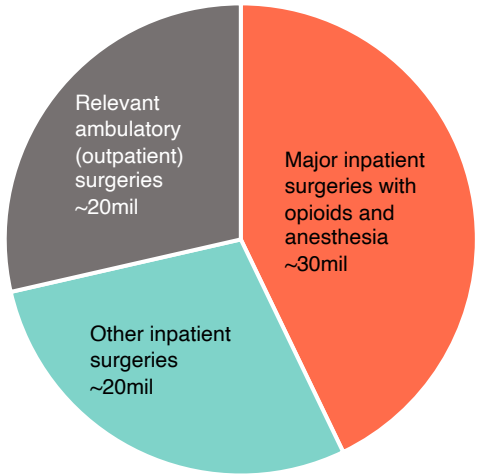
Multiple Products Offer a Diversified Pathway to a $1Billion+ Market Opportunity

Post-Surgery

- Sales potential (yr 5) $650M to $1.5B+
- High incidence of respiratory depression episodes, significant cost burden
- Limited treatment options available

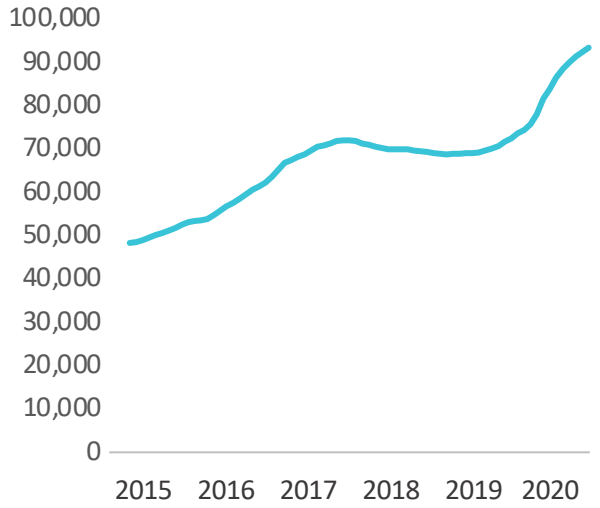
70+ million procedures performed annually in the US[1,2]



Drug Overdose

- Sales potential (yr 5) of $350M to $500M+
- Drug overdose deaths at record high
- Clear unmet medical need for poly-substance overdose and managing withdrawal

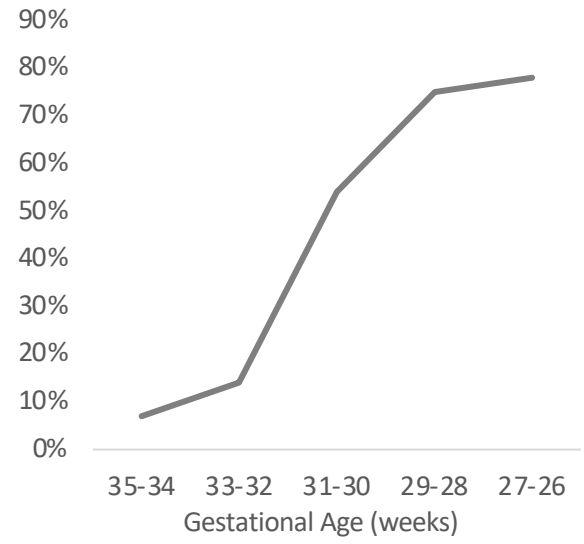
Number of Drug Overdose Deaths US CDC, 12 Months-ending Dec. 2020[3]



Apnea of Prematurity

- Sales potential (yr 5) $250M to $500M+
- Steady prevalence of ~10% for preterm birth
- Treatment to be used as monotherapy and in conjunction with caffeine

Frequency of Apnea of Prematurity[4]



[1] Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic, Anesth Analg. 2017 November ; 125(5): 1733–174
[2] Ambulatory Surgery Data From Hospitals and Ambulatory Surgery Centers: United States, National Health Statistics Reports, Number 102, February 28, 2017

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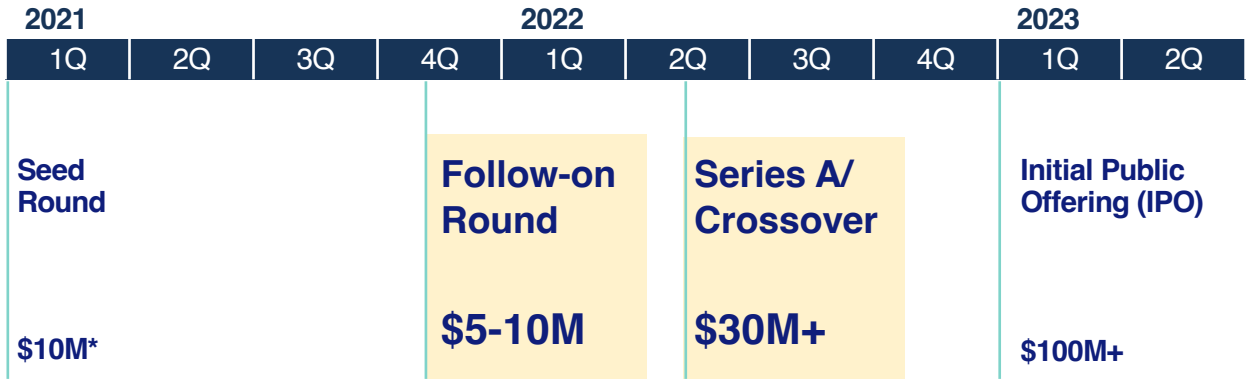
[3] US HHS, Centers for Disease Control and Prevention (CDC), Provisional Drug Overdose Death Counts 12-month ending Dec. 2020, data available as of August 2021
[4] Bohin, S., Field, D.J., The Epidemiology of Neonatal Respiratory Disease, Early Human Development, volume 37, Issue 2, May 1994,

Enalare In-process of Raising Capital to Fund Development of the Three Initial Products

Current Capital Raise



Capital Round	**Seed Round**	**Follow-on Round**	**Series A/ Crossover**	**Initial Public Offering (IPO)**
Target Amount	**$10M***	**$5-10M**	**$30M+**	**$100M+**
Key Capital Expenditures	• FDA reengagement • API production • Clinical supply • Clinical protocol development • Formulation development	• Clinical study 108 • IM formulation testing • Bolus and IV GLP Tox/PD studies • Post-Op development plan • AoP filings (Orphan, RPD) • Additional patent filings	• R&D expansion • Drug Overdose Phase II • Post-op Phase II • AoP preclinical study • Ex-US development • Pipeline expansion	

*Exceeded original target of $3-5mil

Key Catalysts by 1H 2022

- Clinical Study 108 results
- Intramuscular Formulation Animal results
- Additional Preclinical GLP toxicology results
- Alignment with FDA on Post operative development plan
- Apnea of Prematurity animal proof-of-concept
- Expanded patent portfolio

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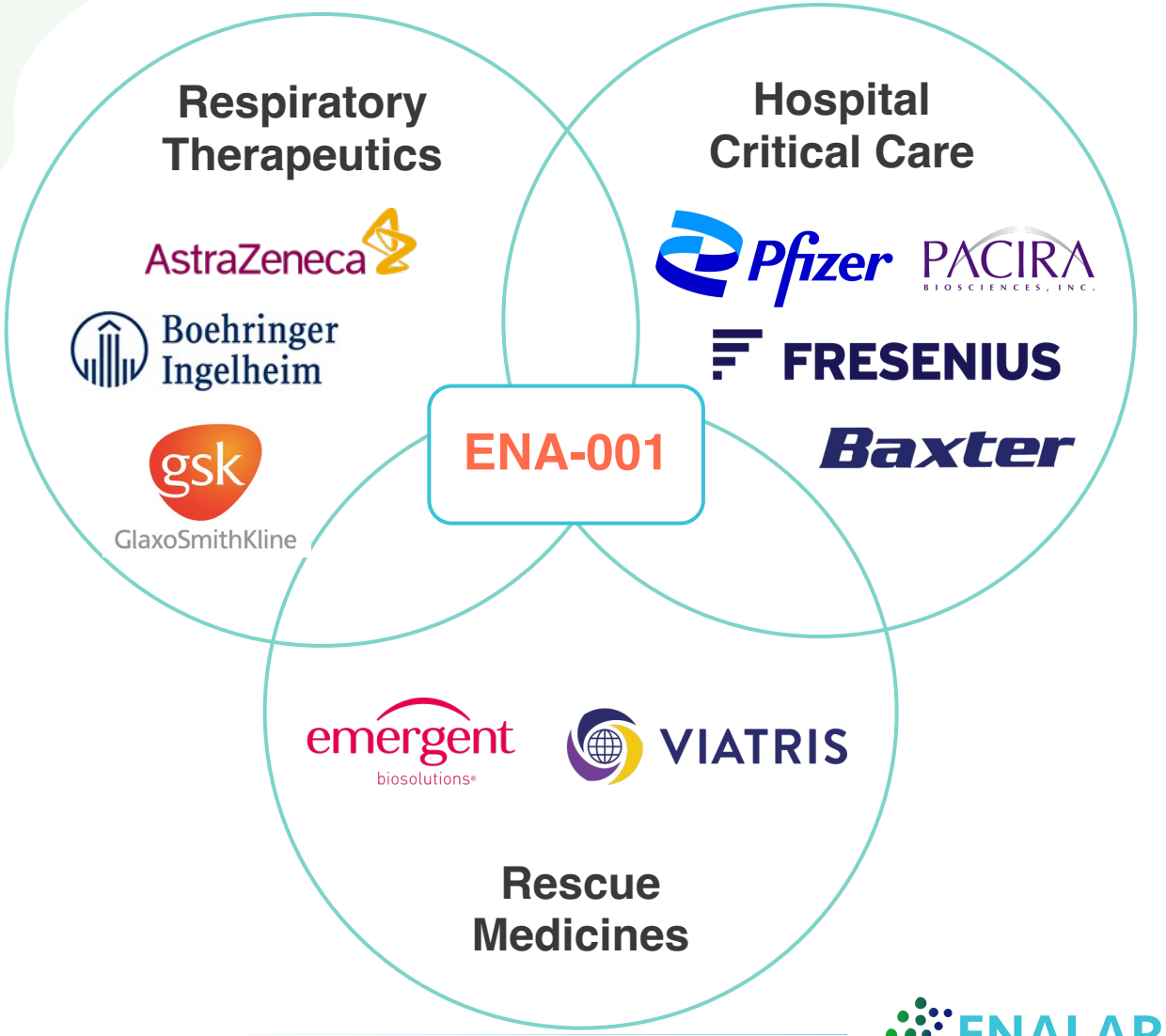
ENA-001's Broad Applications Span Several Segments of the Healthcare Market



Healthcare categories:

- Respiratory Therapeutics
- Hospital Critical Care
- Rescue/Emergency Medicine

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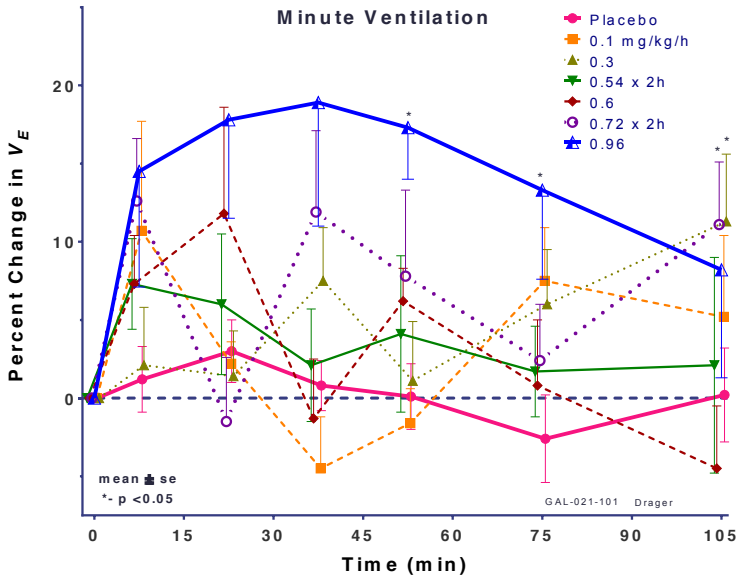
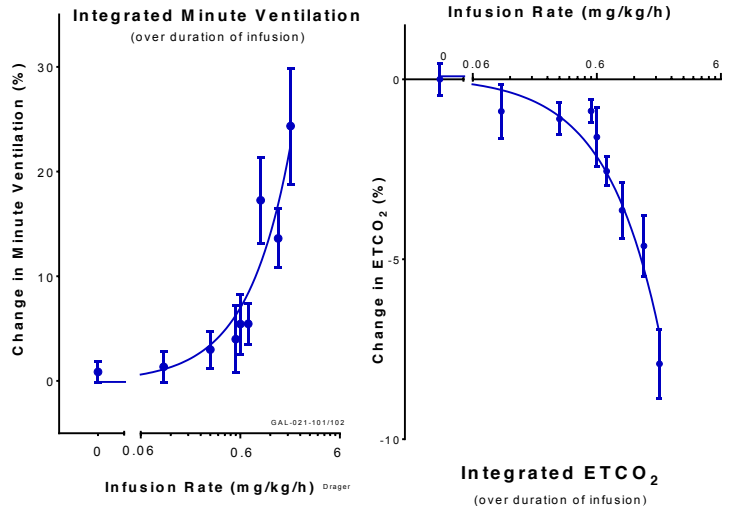
Clinical Study 101/102: Two Rising Single Dose Studies

- Repeated single-dose designs in healthy volunteers
  - Dose range: 0.1 to 1.92 mg/kg/h
- Safety - clean to ~1.1 mg/kg/h
  - Hyperventilation and hypocapnia in 2 subjects at 1.92 mg/kg/min
  - $ETCO_2$ -↓to 22 and 29 torr
  - IV site burning sensation (partially pH - related)
  - GI (N/V) – 4 subjects (top 2 doses)
  - Clinical chemistries – no change
- Pharmacodynamic (PD)
  - Increasing Minute Ventilation and decreasing $ETCO_2$
- Pharmacokinetic (PK)
  - Rapid rise and decline with infusion – Terminal half life (t1/2) of 5.6 hours





Minute Ventilation is defined as the total volume of gas entering (or leaving) the lung per minute and is calculated as the product of tidal volume and respiratory rate

$ETCO_2$: End Tidal CO_2. Maximal concentration of carbon dioxide (CO_2) at the end of an exhaled breath

Clinical Study 104: Proof-of-Concept Study Design with an Opioid

Goal: Test ENA-001 IV under challenging conditions that simulate post-surgical care

- High carbon dioxide (also desensitizes ventilatory control arc to drugs)
- Opioid doses that cause moderate to severe respiratory depression
- Concomitant anti-emetics (required by opioid use)
- No interference with opioid analgesia

Period	Part 1	Part 2 (+ analgesia testing)
1	Baseline (n=12)	Baseline (n=8)
2	CO_2 increased and clamped	Ambient air
3	Alfentanil (titrated) and continued	Same drug doses
4	ENA-001 at 0.4 mg/kg/hr	Same drug doses
5	ENA-001 at 1.1 mg/kg/hr	Same drug doses
6	Alfentanil increase X 2	Same drug doses
7	Continue CO_2 clamp & stop drugs	Ambient air
Respiratory parameters measured on last 10 min of each 30+ minute period		

Design: Double-blind, placebo-controlled, 2-part, 4-period crossover study in 23 healthy subjects

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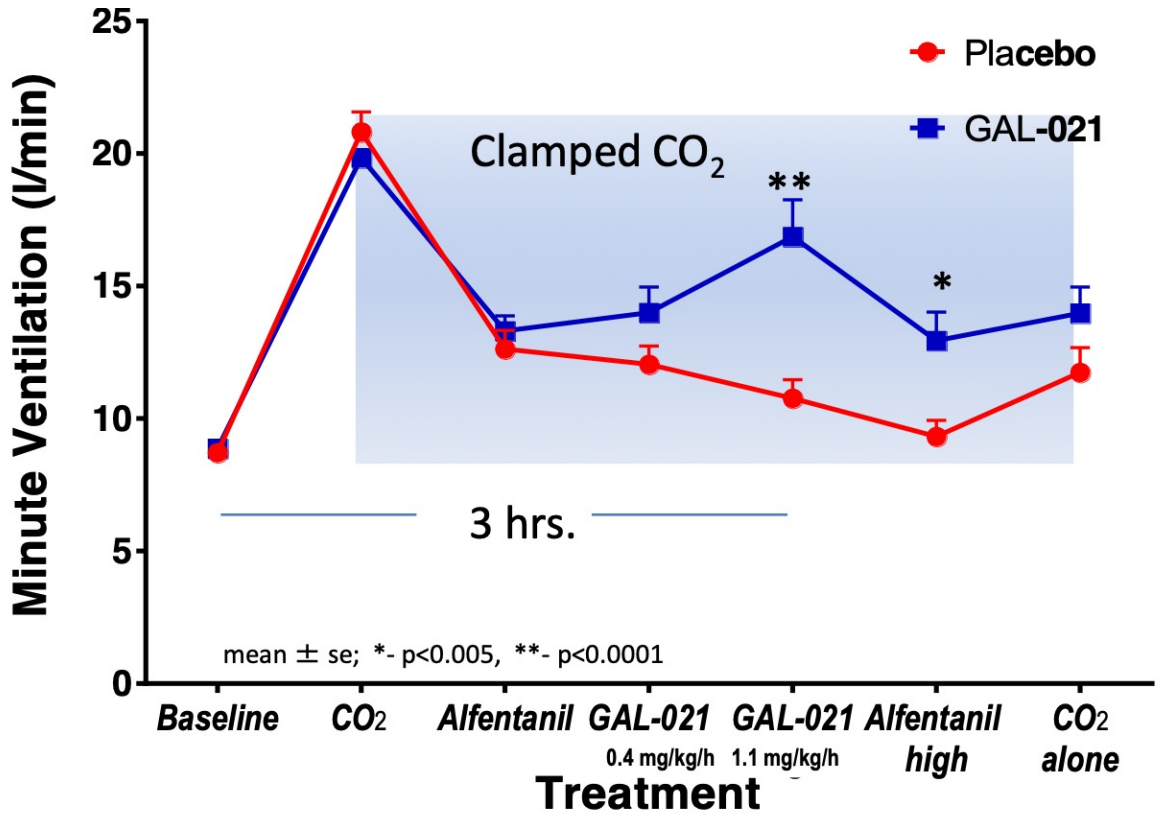
Clinical Study 104: Respiratory Stimulatory Effects in Subjects with Impaired Respiratory Drive

1. Starting baseline
2. Minute ventilation increased rapidly with CO_2 administration to ≈ 20 l/min
3. Alfentanil administration decreased CO_2 - stimulated minute ventilation by 64% which further declined during the subsequent segments with placebo treatment
4. Low dose ENA-001 (0.4 mg/kg/h) tended to increase minute ventilation (9.8% vs. placebo, p ≈ 0.07)
5. High dose ENA-001 (1.1 mg/kg/h) further increasing minute ventilation (21.4%, p < 0.0001)
6. Alfentanil and infusion rate increase, minute ventilation declined for both GAL-021 and placebo while statistically significant separations continued
7. Stop Alfentanil and ENA-001 administration



GAL-021 = ENA-001

Minute Ventilation is defined as the total volume of gas entering (or leaving) the lung per minute and is calculated as the product of tidal volume and respiratory rate

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Clinical Study 106: Rising Multiple Dose 5-day Safety Study of ENA-001

Objectives: Safety, Tolerability, Pharmacokinetics (PK)

- Standard Double Blinded, Placebo Controlled Study
- Infusions: 12 hours x 5 days
- Three Dose Levels (0.125, 0.25, 0.5 mg/kg/h)
- n= 28 subjects

	Study 106 Results
Safety & Tolerability	• Well tolerated except for infusion site burning sensation and local phlebitis after several days of the infusions • CV parameters similar (corrected for baseline) – Blood pressure transient post-infusion increase – Cardiac intervals unchanged • Endocrine-metabolic parameters similar to placebo
Pharmacokinetics (PK)	• Similar Days 1 and 5 • "well-behaved" PK

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Clinical Study 108 Underway with Interim Readout in early 2022

ENA-001-108: A Double Blinded, Placebo Controlled, Crossover Infusion Study of Respiratory Pharmacodynamics of ENA-001 in Conjunction with Propofol, Hypoxia, and Hypercapnia

Expected outcome highlights:

- Demonstrate ENA-001 as a reversal agent for respiratory depression associated with propofol under hypoxic and hypercapnic conditions
- Validation of agnostic respiratory stimulant claim
- Support potential Breakthrough Therapy designation

Low and high doses of ENA-001 in conjunction with low and high doses of propofol to determine:

- Safety and tolerability of ENA-001
- Ventilatory response
- PK parameters
- PK-PD relationship of the ventilatory responses

Study details:

- Conducted by Dr. Albert Dahan at Leiden University Medical Center in the Netherlands
- Protocol approved by the Internal Review Board (IRB) and the Competent Authority in the Netherlands

Current status

- First subject dosed October 25th
- Study progressing well, 8 subjects dosed to date
- No significant reported adverse events
- Interim analysis due 1st week of January 2022

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Post Surgery Respiratory Depression - Risk for Patients and Driving $Billions in Healthcare Costs

Up to 36% of patients are high risk of respiratory depression following surgery[1]

Respiratory depression occurs across the hospital setting	Current treatment options are limited	Impacting patient outcomes and cost of care
• Operating Room (OR) • Post Anesthesia Care Unit (PACU) • General Floor • Intensive Care Unit (ICU)	• Oxygen supplementation • Reduce analgesia/ administer naloxone • Positive pressure ventilation (CPAP) • Re-Intubation/ventilation	• Higher rate of mortality • Longer hospital stays • Increased ICU admissions • Poor pain management • High cost of treatment

Need for a new standard of care: ENA-001 agnostic respiratory stimulant

✓ Improves respiration ✓ Fast onset ✓ Safe & tolerable ✓ Does not impact analgesia

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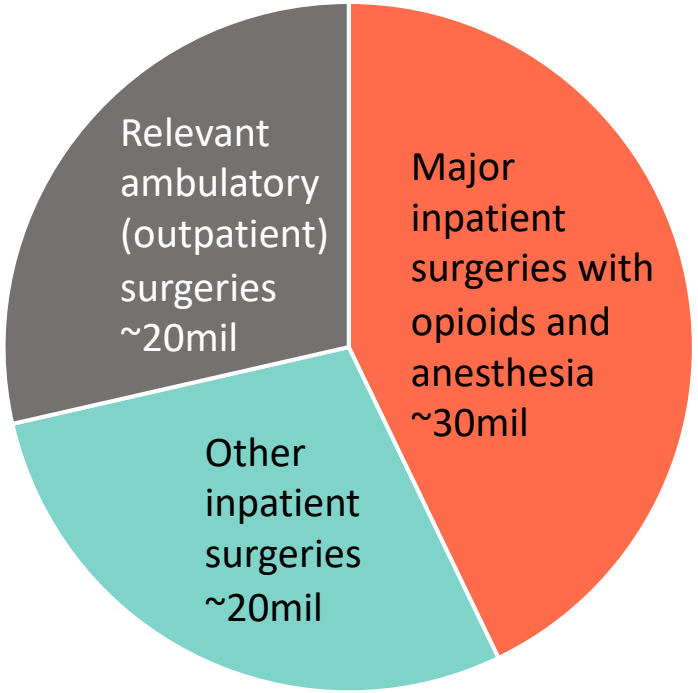
[1] Prediction of Opioid-Induced Respiratory Depression on Inpatient Wards, A. Khanna, et al. Anesthesia & Analgesia: October 2020

Large Post Surgery Market Opportunity with Compelling Health Economics

70+ million procedures performed annually in the US



50 million inpatient procedures[1]

20 million outpatient procedures[2]

Respiratory Distress presents a major cost burden on hospitals[3,4,5,6]

Incremental hospital stay with a respiratory event	• 5-9 days • 2-3X multiple
Incremental costs with a respiratory event	• Avg. $50-60K/ hospitalization • 4X+ multiple
ICU Admissions (unplanned)	• 17-47% have a respiratory indication
Mechanical ventilation costs	• $27 billion annually (1/3 of ICU costs)

[1] Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic, Anesth Analg. 2017 November ; 125(5): 1733–174
[2] Ambulatory Surgery Data From Hospitals and Ambulatory Surgery Centers: United States, National Health Statistics Reports, Number 102, February 28, 2017
[3] Characterisation and monitoring of postoperative respiratory depression: current approaches and future considerations, S. Ayad, *et al.* British Journal of Anaesthesia, 123 (3): 378e391, 2019
[4] Association of Opioids and Sedatives with Increased Risk of In-Hospital Cardiopulmonary Arrest from an Administrative Database, February 25, 2016
[5] Premier Market Research Hospital Database Study, Galleon Pharmaceuticals, 2012
[6] Rao, et al."Postoperative Respiratory Impairment Is a Real Risk for Our Patients: The Intensivist's Perspective," Anesthesiology Research and Practice, vol. 2018

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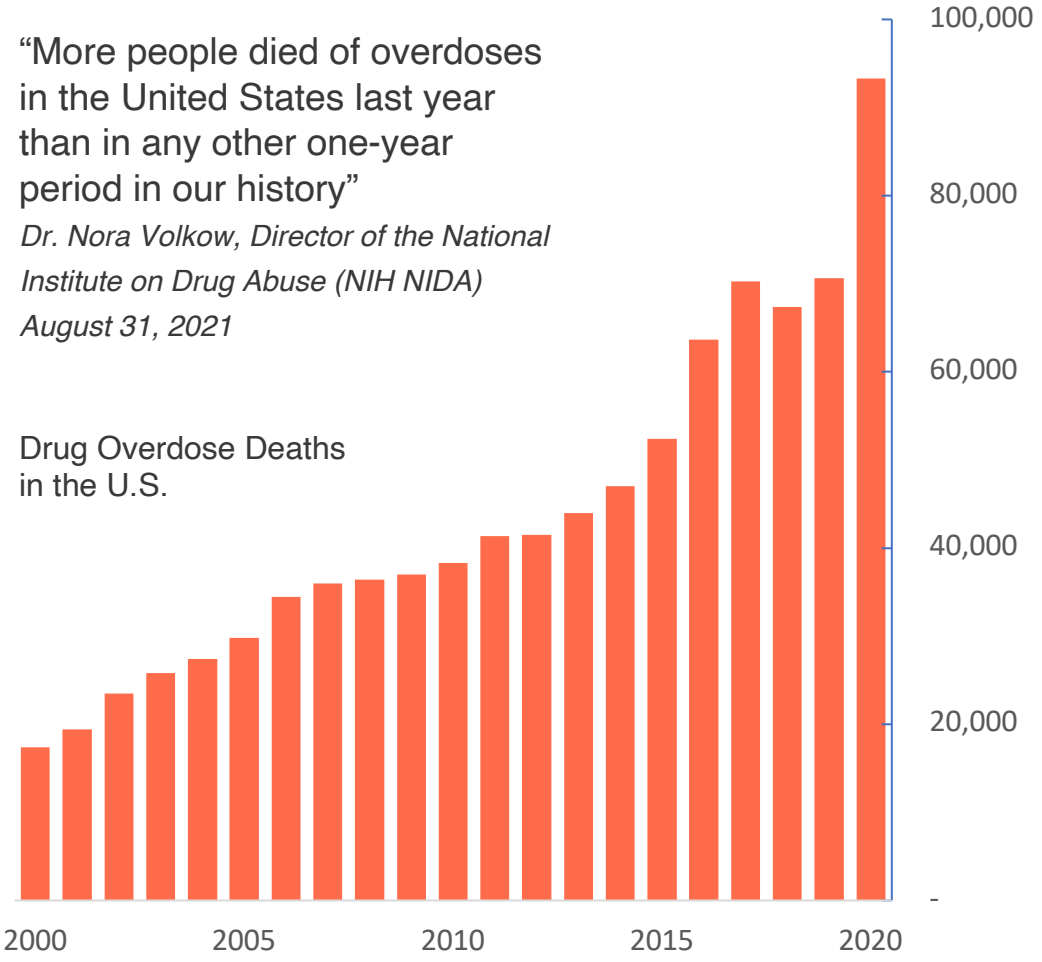
The Rapidly Escalating Drug Overdose Epidemic - Dire Need for Innovative Treatment Options

- COVID-19 has only further accelerated this trend, with 95,230 overdose deaths reported by the CDC[1]
- Poly-pharmacy (multiple drug) abuse is estimated at greater than 40% and rising[2]
- For every drug overdose that results in death, there are many more non-fatal overdoses
  - Approximately 20mil users misuse opioids and other depressant drugs annually[3]
  - Significant burden on healthcare systems, hospital resources and payors[4]
- Naloxone (approved in 1971) is the only marketed reversal agent – problematic and incomplete:
  - Efficacy limited to opioid overdose
  - Agitated patients consume significant ER resources

"More people died of overdoses in the United States last year than in any other one-year period in our history"

Dr. Nora Volkow, Director of the National Institute on Drug Abuse (NIH NIDA)

August 31, 2021



[1] US HHS CDC, 12-month ending Jan. 2021, data available as of Sept. 2021
[2] NIH National Institute on Drug Abuse
[3] Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health, SAMHSA, U.S. Department of Health and Human Services
[4] Opioid Overdoses Costing U.S. Hospitals an Estimated $11 Billion Annually, Premier Inc, January 2019

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Current Treatments for Drug Overdose are Inadequate

Drug overdose assessment - many unknowns

- ? Drugs involved, poly-pharmacy, potency
- ? Medical history, concomitant conditions
- ? Potential for agitation/combativeness and other withdrawal symptoms

Treatment needs:

- ✓ Effective agnostic ventilatory stimulant for multiple drug classes
- ✓ Fast onset, adequate duration of action
- ✓ No precipitated withdrawal or reversal of analgesia
- ✓ Favorable safety profile across patient types

"I just need to make sure the patient is breathing and then I can focus on treatment."

Emergency Medicine Physician

Approved products	Indication	Product Issues
Naloxone (Narcan) approved 1971	Opioid overdose	• Opioid withdrawal symptoms • Removes pain relief • Potential agitation • Short duration
Flumazenil (Romazicon) approved 1991	Benzodiazepine overdose	• Contraindications and the possibility of it causing severe adverse effects including seizures, adverse cardiac effects, and death
Doxapram (Dopram) approved 1965	Respiratory and CNS depression due to drug overdosage	• Side effects include high blood pressure, panic attacks, rapid heart rate, tremor, sweating, and vomiting. Convulsions reported. • Contraindicated in people with coronary heart disease, epilepsy, and high blood pressure.

Opioids: fentanyl, hydrocodone, oxycodone, morphine, etc.
Benzodiazepines: diazepam (Valium), alprazolam (Xanax), clonazepam (Klonopin), etc.

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Apnea of Prematurity - a Life Threatening and Debilitating Condition for Neonates

Apnea of Prematurity

- A developmental disorder characterized by cessation of breathing for > 20 seconds or <20 seconds accompanied by a bradycardia or hypoxemia
- Can lead to respiratory failure and the need for mechanical ventilation
- AoP may increase the risk of impaired neurological development and/or retinopathy of prematurity
- Significant cost burden associated with treatment and an apnea-free period of 5-8 days generally required for NICU discharge[1]

✓ Large global market opportunity

- US preterm birth rate remains steady at ~10%[2], globally ~ 15 million babies born prematurely on an annual basis
- High incidence of breathing disorders in premature infants
  - Approximately 25% of infants born preterm experience AoP[3]
  - All infants experience periodic breathing with brief apneas[4]

✓ Unmet medical need

- International guidelines favor non-invasive respiratory support, ventilating preterm infants can be associated with severe negative pulmonary and extrapulmonary outcomes
- Caffeine citrate is the standard of care, though efficacy of approximately 60% for treatment of AoP[5]

✓ Potential eligibility for development incentive programs

- Orphan Drug Designation – tax credits on development costs, 7-year market exclusivity period, FDA assistance on protocols
- Rare Pediatric Disease – Priority Review Voucher (PRV)

[1] Eric C. Eichenwald, Comitte on Fetus and Newborn Pediatrics Jan 2016, 137 (1) e20153757; DOI: 10.1542/peds.2015-3757
[2] Hamilton, B., et. al., U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System Report 012, May 2021
[3] Merck Manual, Arcangela Lattari Balest, 2019, Pediatrics, Respiratory Problems in Neonates, Overview of Perinatal Respiratory Disorders
[4] Martin R., et al., Apnea of Prematurity, Pediatric Respiratory Reviews, 2004, 5 (Supplement A), S377-382
[5] CAFCIT Prescribing Information, Nov 2009.

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Enalare is Well Positioned to Capitalize on Strong Momentum and Create Significant Sustained Enterprise Value

✓ Proven top-tier team	• Demonstrated ability to develop and launch blockbuster products with consistent value creation • Industry leading scientists and advisors
✓ Significant medical need	• Convergence of health emergencies with commonality of respiratory depression • Critical need for a safe, agnostic respiratory stimulant in multiple treatment settings
✓ Breakthrough Science	• First-in-class NCE compounds with a novel mechanism-of-action • Potential to be first new product approved in several decades across multiple indications
✓ Robust proof-of-concept	• Positive safety and efficacy results across more than four human trials • Strong pre-clinical platform including extensive toxicology studies across multiple animal species
✓ Large market opportunities	• Broad medical and health economic benefits driving $1.5B+ sales potential* • Global exclusivity extending into the 2040s

*Enalare Therapeutics internal analysis

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For more information:

www.enalare.com