



Enalare Therapeutics Inc.

Developing and commercializing novel therapies to address the
national health crisis of Acute Respiratory Depression

December 2020

Contact: Daniel Motto, Chief Business Officer
dmotto@enalare.com

Confidentiality & Disclaimer

This presentation (this “Presentation”) is being furnished to you on a confidential basis to provide preliminary summary information regarding Enalare Therapeutics Inc., a Delaware corporation (the “Company”). Certain information contained in this Presentation or otherwise provided to you is nonpublic, confidential and/or proprietary in nature. By accepting this Presentation, you agree to keep the information contained herein and any other information provided by the Company or its representatives strictly confidential.

This Presentation is the sole property of the Company. The information contained herein has not been released publicly. Neither the Company nor any of its affiliates, nor any of their respective shareholders, directors, officers, employees, consultants, agents, advisors, or representatives, makes any representation or warranty as to the accuracy or completeness of the information contained in this Presentation. The sole purpose of this Presentation is to assist persons in deciding whether they wish to proceed with a further review of a potential transaction involving the Company and is not intended to be all-inclusive or to contain all the information that a person may desire in considering such a potential transaction. It is not intended to form the basis of any investment decision or any other decision in respect of the proposed transaction.

This Presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of securities in any jurisdictions in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. The information contained in this Presentation or otherwise provided to you is provided for informational purposes only, does not recommend the purchase or sale of any security, is not complete and does not contain all material information about the Company, including important disclosures and risk factors associated with an investment and is subject to change without notice.

The estimates and projections of future performance set forth in this Presentation are based on numerous assumptions about sales, margins, competitive factors, industry performance and other factors which cannot be predicted. Although the Company believes that such assumptions are reasonable, they may be incomplete or incorrect, and other events and circumstances may occur. Therefore, the actual results of operations are likely to vary from the projections and the variations may be material and adverse. The projections should not be regarded as a representation or prediction that the Company will achieve or is likely to achieve any particular results.

This Presentation includes “forward-looking statements.” The Company’s actual results may differ from its expectations, estimates and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as “expect,” “estimate,” “project,” “budget,” “forecast,” “anticipate,” “intend,” “plan,” “may,” “will,” “could,” “should,” “believes,” “predicts,” “potential,” “continue,” and similar expressions are intended to identify such forward-looking statements. These forward-looking statements include, without limitation, the Company’s expectations with respect to future performance. These forward-looking statements involve significant risks and uncertainties that could cause the actual results to differ materially from the expected results. Most of these factors are outside the Company’s control and are difficult to predict. Important factors that could cause actual results to differ materially from expectations include, but are not limited to: (i) business, economic and capital market conditions, (ii) current or future laws or regulations and new interpretations of existing laws or regulations, (iii) legal and regulatory requirements, including receipt of timely regulatory approvals, (iv) the Company’s ability to attract, retain and motivate qualified personnel, (v) competition in the Company’s industry, (vi) the potential impacts of the COVID-19 pandemic on the Company’s business operations, including its supply chain, and its ability to raise capital, (vii) the ability to obtain additional financing on reasonable terms or at all, and (viii) market acceptance of the Company’s products, and (ix) the Company’s ability to successfully maintain and enforce its intellectual property rights and defend third party claims of infringement of their intellectual property rights. The Company cautions that the foregoing list of risk factors is not exclusive of all potential risk factors. The Company cautions readers not to place undue reliance upon any forward-looking statements, which speak only as of the date made. The Company does not undertake or accept any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based. Certain financial information and data contained herein is unaudited and/or was not derived in accordance with United States generally accepted accounting principles (GAAP).

You should not construe the contents of this Presentation as legal, tax, investment or other advice. You should make your own inquiries and consult with your own advisors as to legal, tax, investment, and related matters concerning any proposed transaction with the Company.



Enalare presents a compelling investment opportunity

Poised to fundamentally change clinical practice in the treatment of acute respiratory depression



Significant medical need

- Convergence of health emergencies with commonality of respiratory depression
- Critical need for a safe, agnostic ventilatory stimulant in multiple treatment settings



Robust proof-of-concept

- Positive safety and efficacy results across four human trials
- Extensive pre-clinical platform, including 12 toxicology studies in multiple animal species



Clear & expedient path to market

- Well defined development program with clear endpoints for reversal of respiratory depression
- Initiating registration trials for lead indication – estimate approval in ~ 2 years



Large market opportunities

- Broad medical and health economic benefits driving \$1.5B+ sales potential*
- Novel mechanism-of-action with patent protection through 2031, additional patents pending



Proven top-tier team

- Demonstrated ability to develop and launch blockbuster products with consistent value creation
- Industry leading scientists and advisors



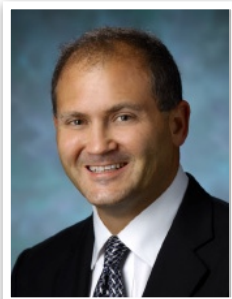
*Enalare internal analysis

Enalare Senior Management & Board of Directors



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 Business Officer

- EVP of 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.

- Eli Lilly & Co
- Board Member:
 - Horizon Pharma
 - Amag Pharma
 - Intercept Pharma
 - Collegium Pharma

Bob Yedid

30 yrs of experience as a buy-side analyst, portfolio manager, private equity investor and investment banker. Currently focuses on providing CEOs and CFOs with strategic advice on key investor issues. Former Board member of The Medicines Co. and Vaxart. MBA Stanford School of Business, BA Yale University.

- LifeSci Advisors
- Principal Capital
- Warburg Pincus
- Bear Stearns & Co (now JPM)

Joseph Petko

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

- Ashford Capital Management
- Merck & Co.



Acute Respiratory Depression – A National Health Emergency

Respiratory Depression

Respiratory Depression is a condition characterized by slow and ineffective breathing resulting in:

- low levels of oxygen (hypoxemia) and/or
- high levels of carbon dioxide (hypercapnia)

If left untreated it can cause life-threatening complications, including death.

Common Causes:

Medications

- Sedative medications
- Narcotics for pain
- Alcohol
- Other substances that depress brain function
- Synergistic effect from drug combinations

Health Conditions

- Obesity and aging
- Viral or bacterial infections (e.g. COVID)
- Neuromuscular diseases
- Sleep apnea
- Chronic lung diseases



Initial Target Markets

Drug overdose

- Substance abuse epidemic accelerating
- US deaths exceeded 70K, record high expected in 2020
- Polysubstance (multi-drug) abuse a growing issue
- Current treatment option is incomplete – only addresses opioid overdose
- Expedited pathway to market

Post-operative care

- Large and growing at-risk populations
- Unmet medical need – very limited treatment options
- 50mil+ surgeries performed annually
- Compelling health economic benefits by reducing ICU/overall hospital length of stay
- Significant long-term commercial potential – US and Ex-US

Respiratory infections

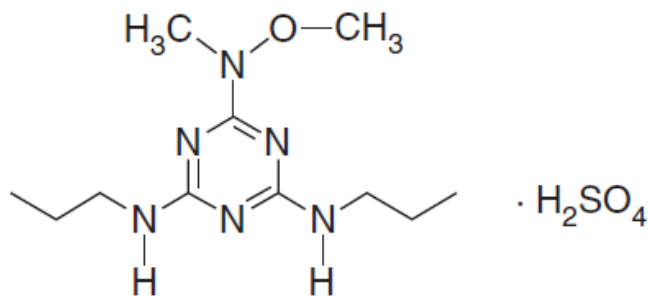
- Acute and chronic respiratory complications associated with infections
- COVID-19 pandemic highlighting risks
- High mortality rate if require ventilator
- Urgent need for new therapies to address on-going incidence and pandemic spikes



ENA-001: A first-in-class New Chemical Entity (NCE)

Agnostic Ventilatory Stimulant

- A new molecule (NCE) with novel Mechanism-of-action (MoA) - Inhibits Big Potassium (BK) ion channels
- It does not interfere with pain suppression or sedation – safely restores respiration without combative withdrawal



ENA-001 hydrogen sulphate salt

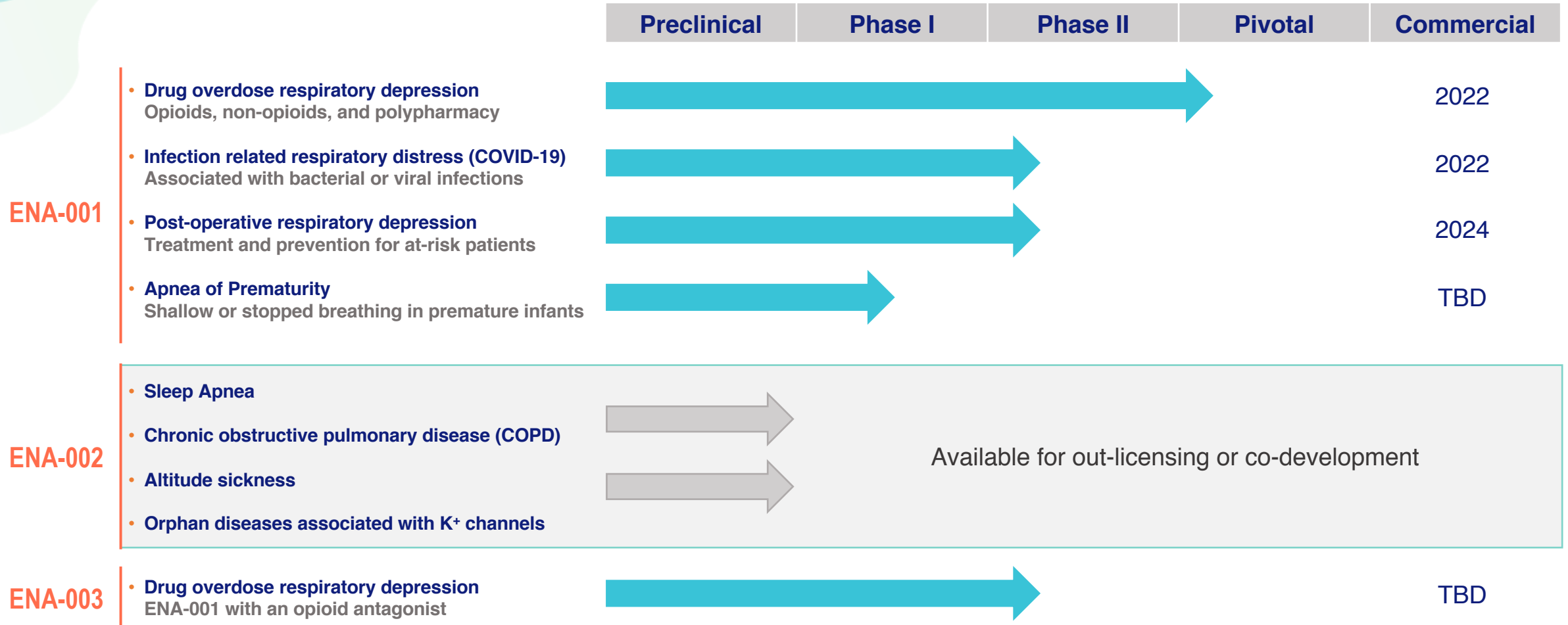
2-N,O-dimethylhydroxylamino-4,6-bispropylamino-s-triazine

Advanced Development Status

- Ready to initiate registration studies in Q2 2021
- Existing human proof-of-concept studies
- Safe and well tolerated
- Strong IP including issued composition-of-matter patents extending through Dec. 2031
- Existing clinically effective formulation with next generation re-formulation underway
- Clear and rapid path to market for lead indication (drug overdose) with potential for accelerated FDA review
- Significant potential for near-term value inflection



Enalare's pipeline has the potential to dramatically improve medical practice and patient outcomes in multiple settings

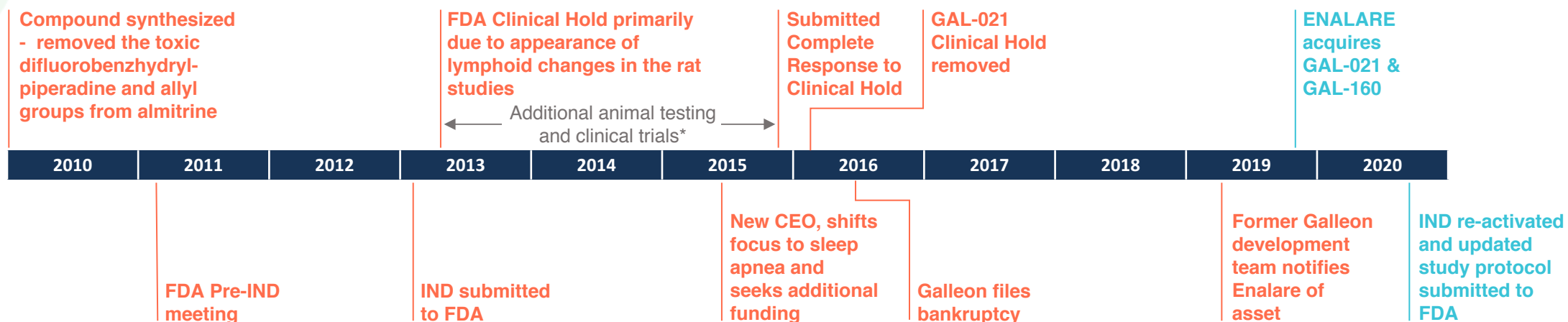


ENA-001/ENA-003: Ex-US geographies available for out-licensing

ENA-001 historical development timeline

\$30+ million invested to-date

Galleon Pharmaceuticals Development of GAL-021 (now ENA-001)



Market Developments

Growing need for a new respiratory stimulant

Obesity and aging population increasing respiratory risks

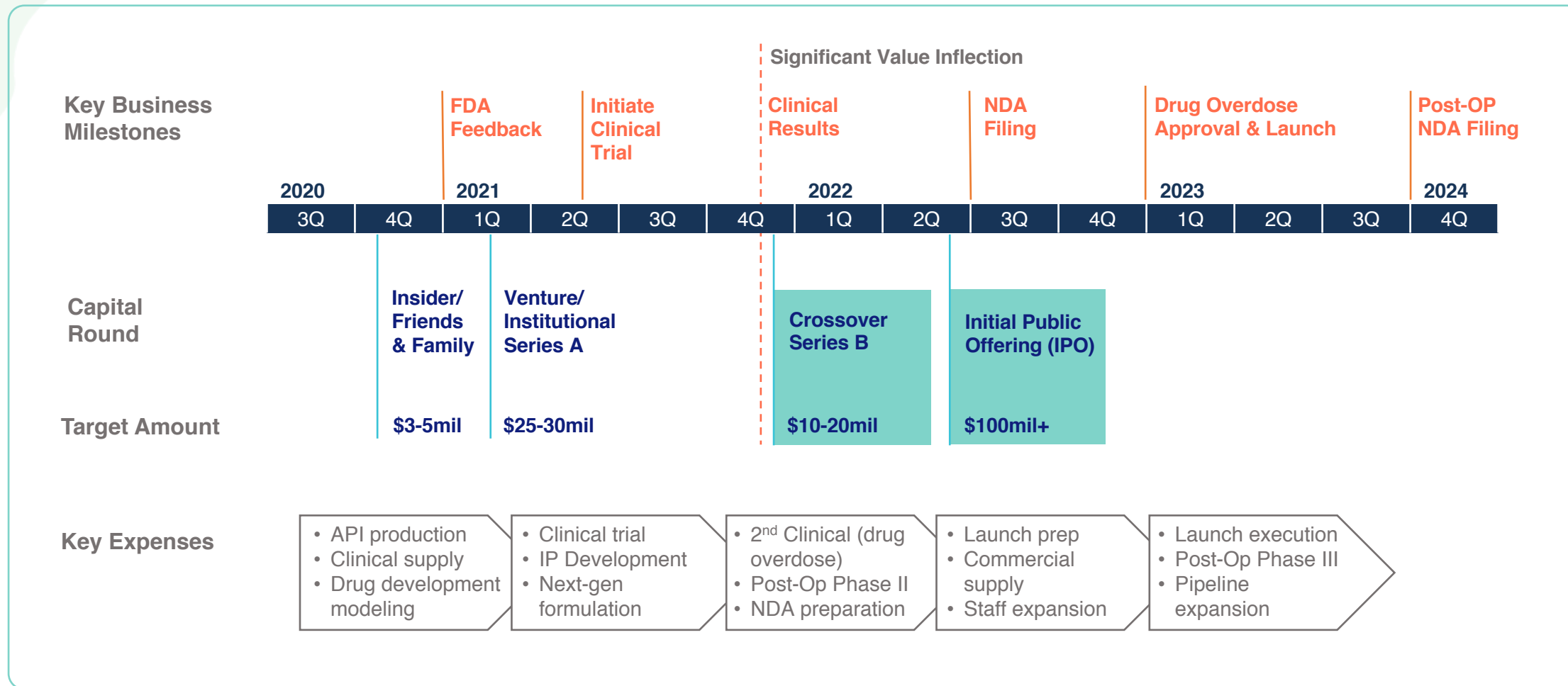
US substance abuse epidemic accelerates

COVID pandemic highlights risks of infection-related respiratory distress

*GAL-021-104 & 106 studies in human approved by the Dutch Early Ethics Committee



Enalare proposed capital plan with key milestones

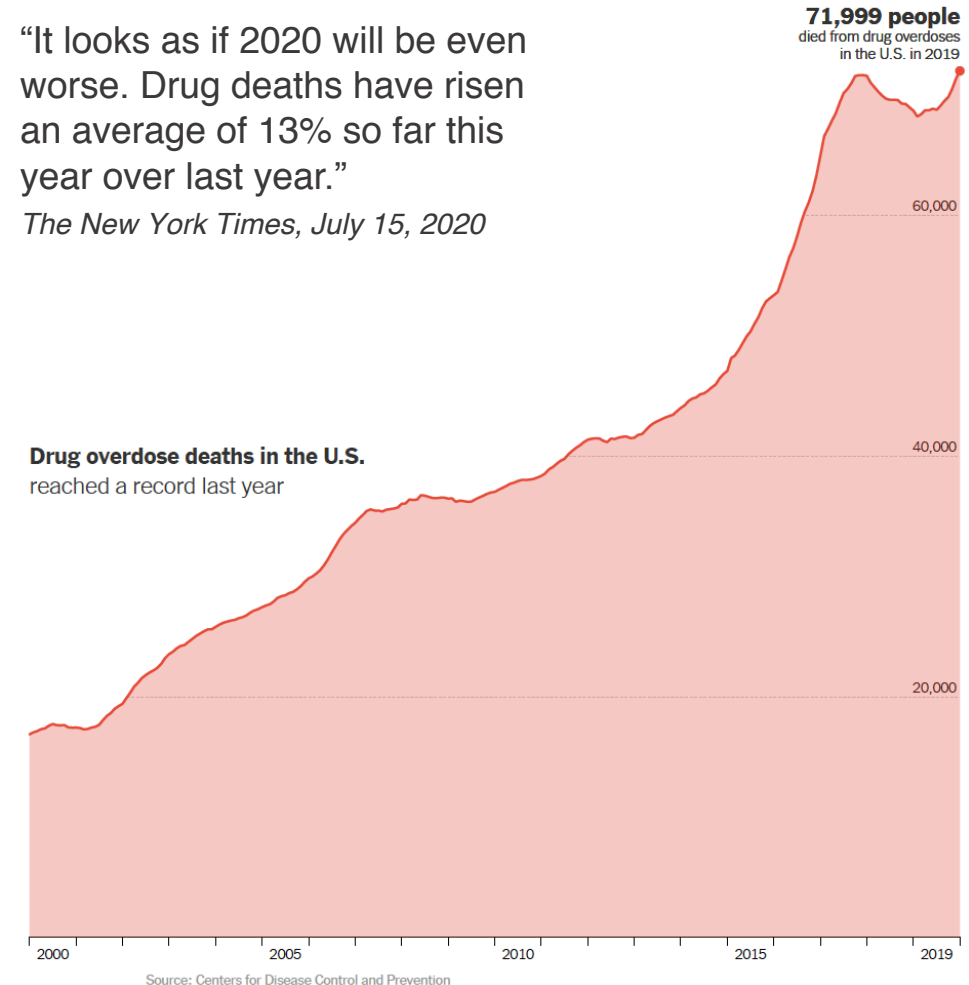


The drug overdose epidemic is escalating and evolving - dire need for an agnostic breathing stimulant

- Drug deaths in the US rose to record levels in 2019
- Early signs indicate that COVID-19 has only further accelerated this substance abuse trend
- Poly-pharmacy (multiple drug) abuse is estimated at greater than 40% and rising¹
- For every drug overdose that results in death, there are many more non-fatal overdoses
 - Approximately 20mil users misuse opioids and other depressant drugs annually²
 - Significant burden on healthcare systems, hospital resources and payors³
- Naloxone (approved in 1971) is the only marketed reversal agent – problematic and incomplete:
 - Efficacy limited to opioid overdose
 - Agitated patients consume significant ER resources

“It looks as if 2020 will be even worse. Drug deaths have risen an average of 13% so far this year over last year.”

The New York Times, July 15, 2020



¹ NIH National Institute on Drug Abuse

² 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

³ Opioid Overdoses Costing U.S. Hospitals an Estimated \$11 Billion Annually, Premier Inc, January 2019

Current treatments for drug overdose are inadequate and ill suited for many treatment scenarios

Drug overdose assessment - many unknowns



- ? Drugs involved, polypharmacy, 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, long 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	Description	Product Issues
Naloxone (Narcan) approved 1971	An opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose	<ul style="list-style-type: none">• Opioid withdrawal symptoms• Removes pain relief• Potential agitation• Short duration
Flumazenil (Romazicon) approved 1991	A benzodiazepine receptor antagonist that is indicated for the reversal of conscious sedation induced with benzodiazepines – it can be used as an antidote for benzodiazepine overdose	<ul style="list-style-type: none">• Contraindications and the possibility of it causing severe adverse effects including seizures, adverse cardiac effects, and death
Doxapram (Dopram) approved 1965	A respiratory stimulant that stimulates chemoreceptors in the carotid bodies. Indicated for drug-induced central nervous system depression and maybe used in patients with mild to moderate respiratory and CNS depression due to drug overdosage	<ul style="list-style-type: none">• Side effects include high blood pressure, panic attacks, rapid heart rate, tremor, sweating, and vomiting. Convulsions have been 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.



Post-operative respiratory distress – Significant risk to patient safety and time delays within surgical theater

Up to 36% of patients are high risk of respiratory depression following surgery¹

Current treatment options are limited

Target properties for a respiratory stimulant therapeutic in the post-operative setting

Post-operative Respiratory Depression

Increasing Severity

1. Check airway for obstructions, verbal & physical stimulation
2. Oxygen supplementation
3. Positive pressure ventilation (e.g. CPAP)
4. Reduce opioid use
5. Administer naloxone and/or flumazenil



Intubation/Ventilator
Risk for patient and significant cost for healthcare system

Desired Properties

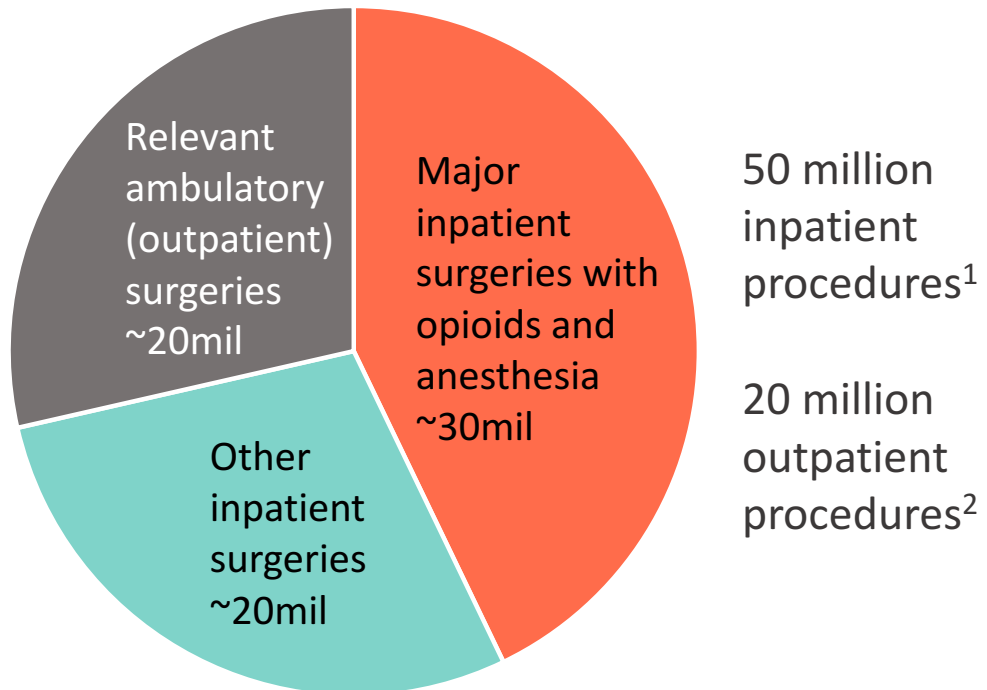
ENA-001

Improves respiration	✓
Does not affect analgesia	✓
Works quickly	✓
Works under conditions of hypercapnia (rising CO ₂)	✓
Pharmacokinetics that allow for easy adjustment	✓
Enhances the ventilatory response under hypoxic conditions (low O ₂)	✓
Works with analgesics and other suppressive classes	✓

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

Large post-operative market opportunity with compelling health economics around treatment of respiratory depression

70+ million procedures performed annually in the US



Respiratory Distress presents a major cost burden on hospitals^{3,4,5,6}

Incremental hospital stay with a respiratory event	<ul style="list-style-type: none">• 5-9 days• 2-3X multiple
Incremental costs with a respiratory event	<ul style="list-style-type: none">• Avg. \$50-60K/ hospitalization• 4X+ multiple
ICU Admissions (unplanned)	<ul style="list-style-type: none">• 17-47% have a respiratory indication
Mechanical ventilation costs	<ul style="list-style-type: none">• \$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



COVID-19 and other viral and bacterial infections leading to lung complications and acute respiratory distress

COVID-19

- The COVID-19 pandemic and others like it will be a concern for the global population in the years ahead
- Over 9 million US infections, deaths now exceed 200,000¹
- Virus expect to persist even with vaccines and improved treatment
- US Federal programs for accelerated pathways to market for new therapeutics:
 - Emergency Use Authorization (EUA)
 - Coronavirus Treatment Acceleration Program (CTAP)
 - Expanded access, Op. Warp Speed



Lung Damage & Respiratory Distress

- COVID-19 can cause lung complications such as pneumonia and, in the most severe cases, Acute Respiratory Distress Syndrome (ARDS)
- Sepsis, and other possible complications of COVID-19, can also cause lasting harm to the lungs
- ~5% of symptomatic COVID-19 patients require admittance to ICU
- Respiratory distress may require CPAP and/or mechanical ventilation for serious cases
- Currently 30-50% mortality rate for patients put on ventilators



Role of ENA-001

- ENA-001 has been called a “pharmacologic ventilator”² and it may have role as an add-on therapy for certain cases
 - Delay or prevent mechanical ventilation
 - Enhance CPAP
 - Aid in weaning off ventilator
- A recent study in COVID patients with a similar compound, almitrine, showed potential beneficial effects
- ENA-001 may improve patient outcomes by a reduction in the risk for oxygen deprivation
- Potential management option for acute and chronic symptoms



¹ Johns Hopkins University, as of Sept 28, 2020

² Joseph F. Cotten, MD, PhD, Editorial, *Anesthesiology*

The complex human ventilatory control system provides multiple pathways for affecting respiration

The chemical ventilation control system relies on a set of chemosensors:

- Brainstem (central chemoreceptors)
- Carotid bodies (peripheral chemoreceptors)

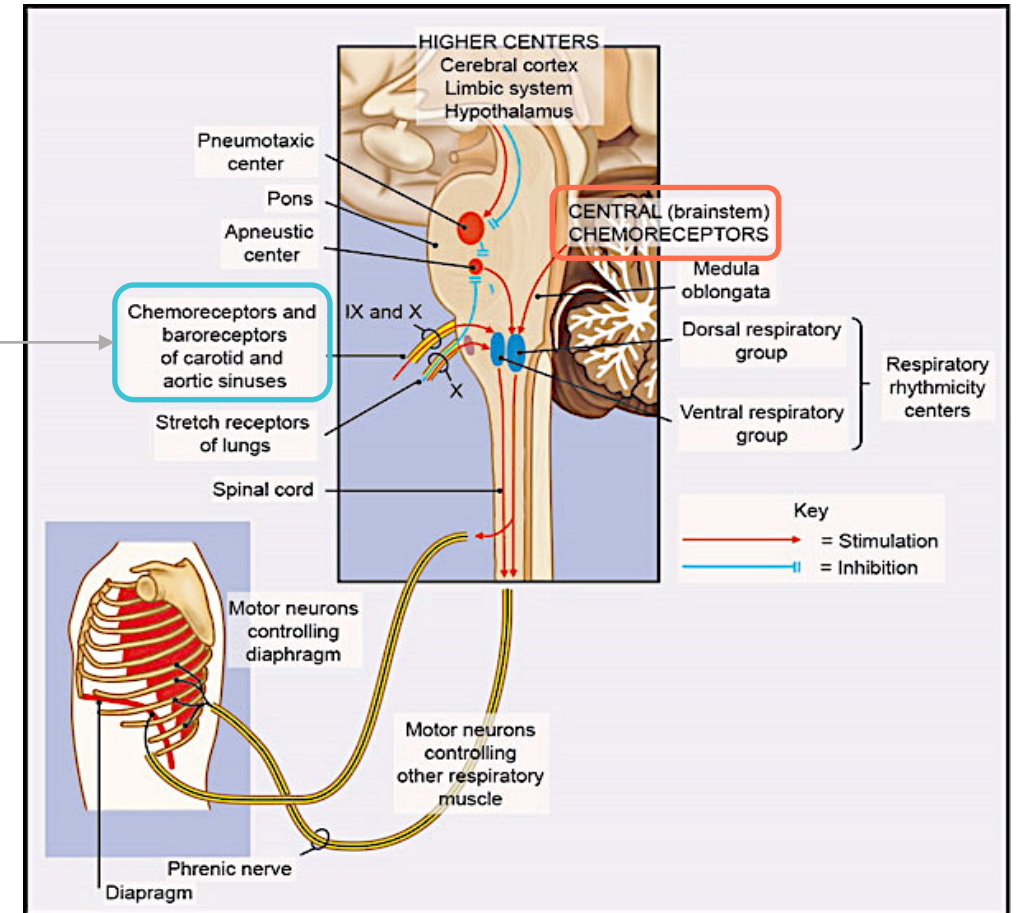
Deviations from chemical cellular homeostasis will typically result in adaptations in breathing frequency and tidal volume.

A variety of different receptors are expressed on respiratory neurons, and their activation or inhibition will directly affect breathing.

Depending on the circumstances, this may be:

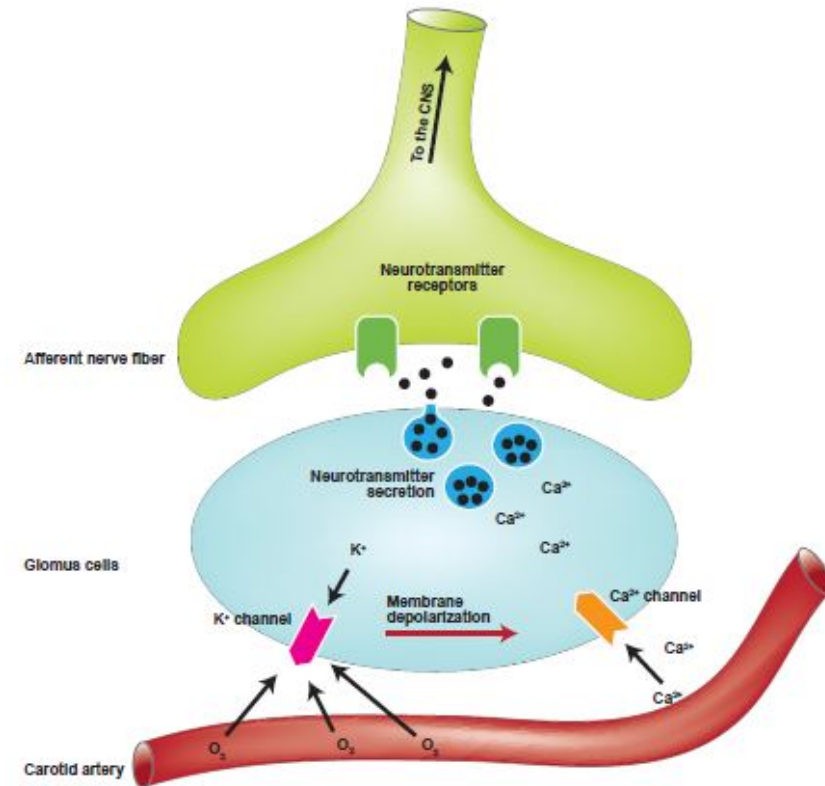
- Advantageous (specific receptor agonists/antagonist may beneficially influence breathing); or
- Disadvantageous (specific drugs may depress ventilation, causing potentially fatal conditions)

ENA-001 affects ventilation via the peripheral chemoreceptor pathways
Safely activating peripheral signals to stimulate breathing



ENA-001's unique Mechanism of Action (MoA) safely stimulates the peripheral breathing components

- ENA-001 acts through large-conductance Ca^{2+} and voltage-activated K^{+} channels in the carotid body to stimulate respiration and increase minute ventilation
- The primary molecular mechanism underlying the ventilatory stimulant effects of ENA-001 appears to be functional inhibition of big potassium (BK) channels.*
- The beneficial effects on respiration are assumed to derive by mimicking the hypoxic (low O_2) inhibition of BK channels: this promotes depolarization of carotid body type I cells and precipitates voltage-gated Ca^{2+} influx where the resultant increase in intracellular Ca^{2+} ($[\text{Ca}^{2+}]_i$) elicits neurotransmitter release to activate sensory afferent discharge to the brainstem (via the carotid sinus nerve) and ultimately to corrective changes in breathing.



Schematic Model of Oxygen Sensing in the Carotid Body

*Exploring secondary MoA



ENA-001's strong intellectual property includes issued composition-of-matter patents

Issued Patents

- **US 9,351,972**
Compounds as Respiratory Stimulants for Treatment of Breathing Control Disorders or Diseases
Includes NCE and Pharmaceutical Composition claims
Expires 11/29/2031 (+ PTE opportunity)
- **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 11/29/2031

Patent and Trademark Applications

- Pending International PCT Application directed to combination therapy for the treatment of opioid overdose, stimulant overdose and polypharmacy overdose. Anticipated expiration of 2040
- Pending U.S. Provisional Application directed to composition and methods for the treatment of respiratory depression in infected patients (including Covid-19). Anticipated expiration of 2041
- 'Enalare' and 'Enalare Therapeutics' trademark applications pending and website domains secured (www.enalare.com)

Patent term extension (PTE) opportunity of up to 5 years on issued patent
Filing strategy in place for future patent opportunities including pharmaceutical formulations, pharmacokinetic/pharmacodynamic profiles, new indications and dosing regimens



ENA-001 shown to be safe and efficacious across four 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

- ✓ Dosing
- ✓ Proof-of-Concept Efficacy
- ✓ Safety & Tolerability

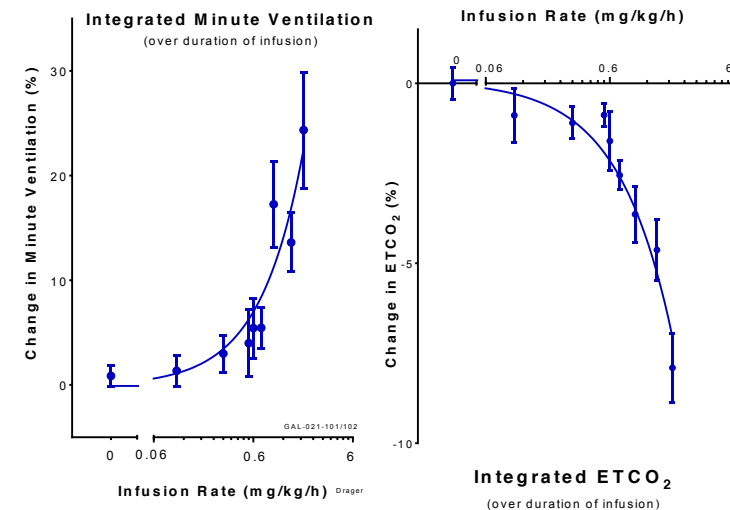
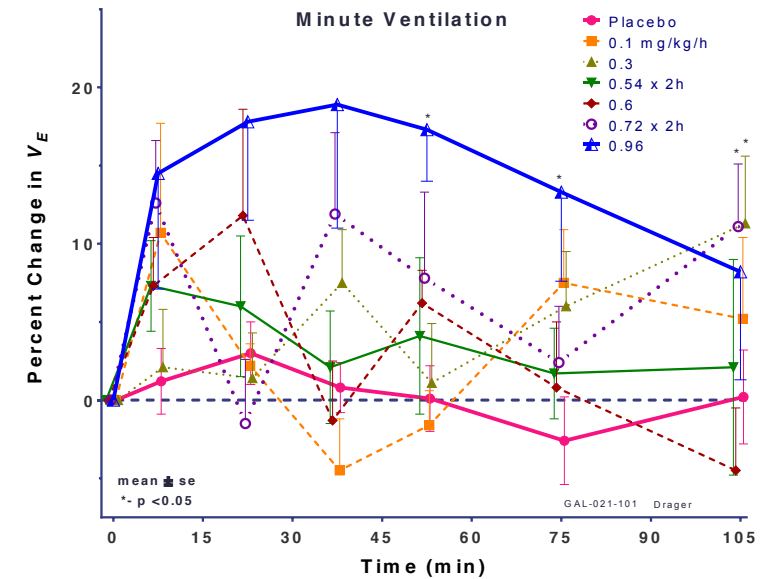


Study 101/102: two rising single dose studies

- Repeated single-dose designs in health 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 ($t_{1/2}$) 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 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



Study 104 proof-of-concept study design with alfentanil

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

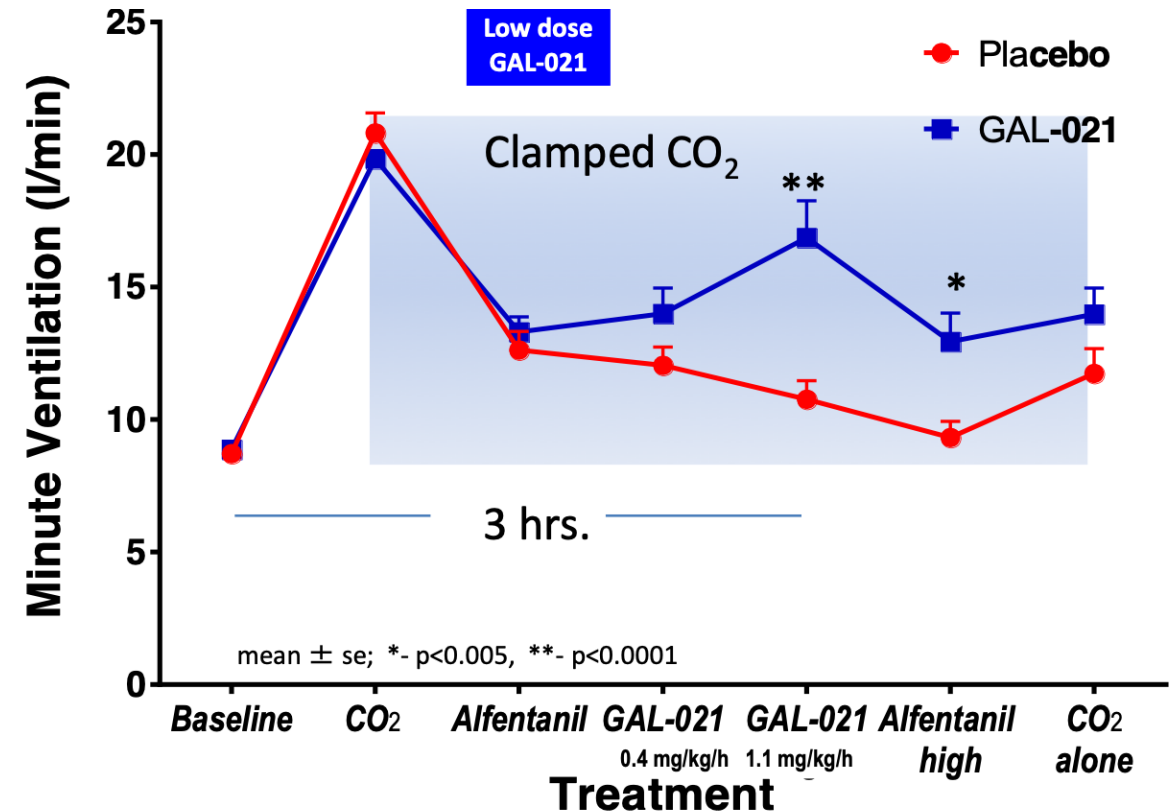
Period	Part 1	Part 2 (+ analgesia testing)
1	Baseline (n=12)	Baseline (n=8)
2	CO ₂ increased and clamped	Ambient air
3	Alfentanil (titrated) and continued	Same drug doses
4	ENA-001 at 0.4 mg/kg/hr	Same drug doses
5	ENA-001 at 1.1 mg/kg/hr	Same drug doses
6	Alfentanil increase X 2	Same drug doses
7	Continue 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



Study 104: part 1 - respiratory stimulatory effects in subjects with impaired respiratory drive

1. Starting baseline
2. Minute ventilation increased rapidly with CO₂ administration to ≈ 20 l/min
3. Alfentanil administration decreased CO₂ - 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, $p \approx 0.07$)
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

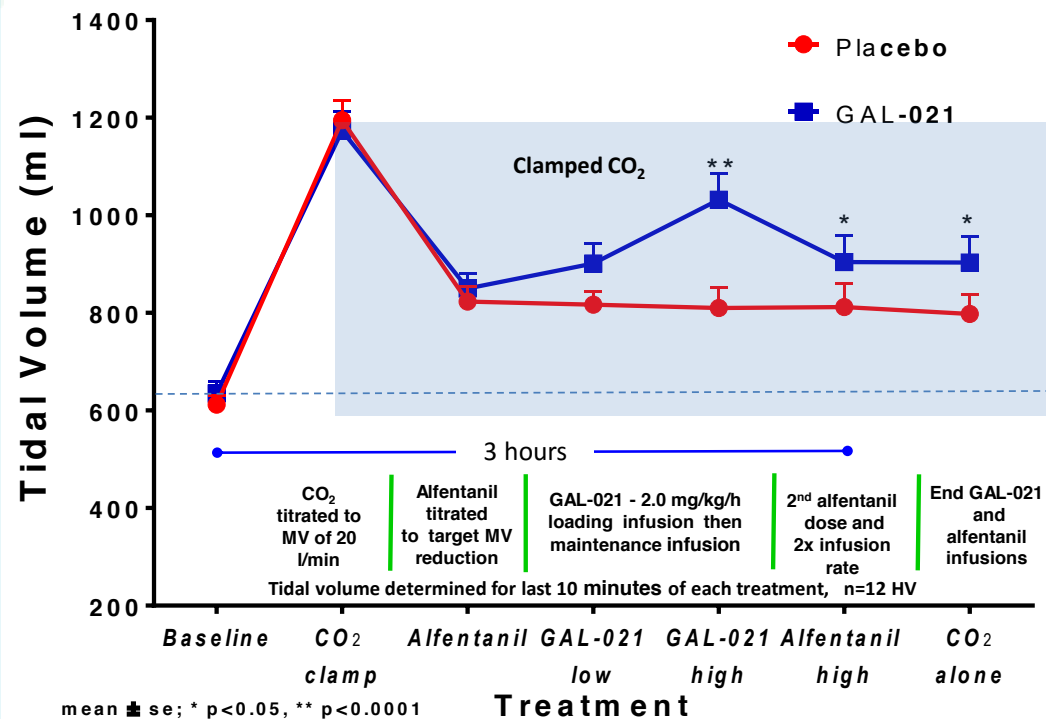


GAL-021 = ENA-001

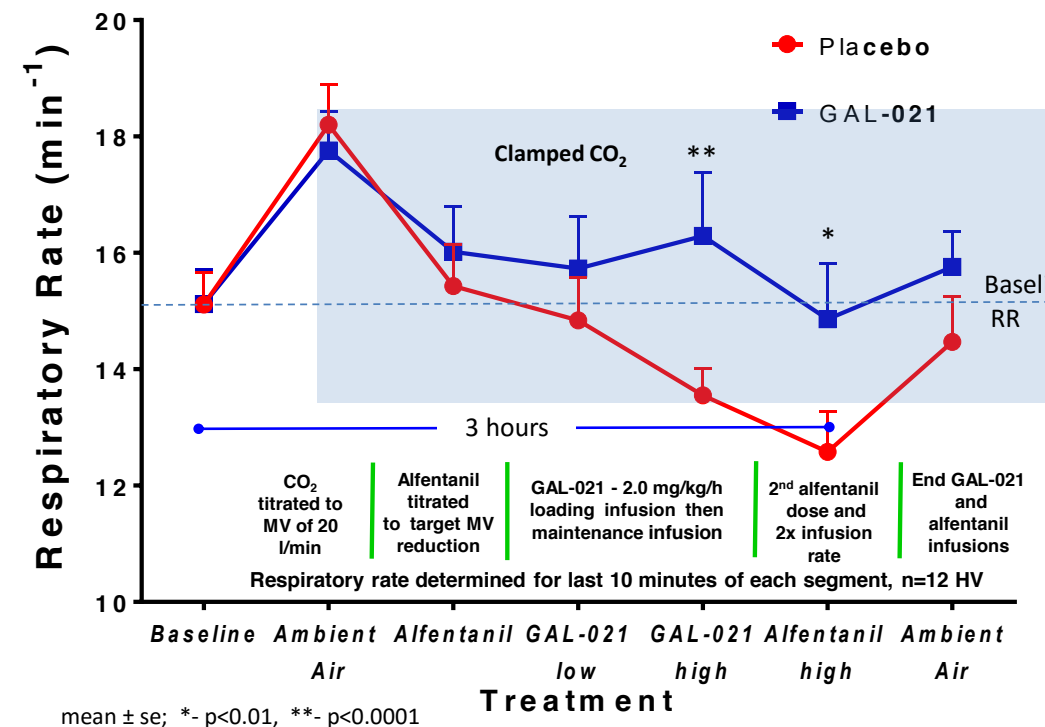


Study 104: part 1 – similar improvements observed for tidal volume and respiratory rate

Tidal Volume



Respiratory Rate

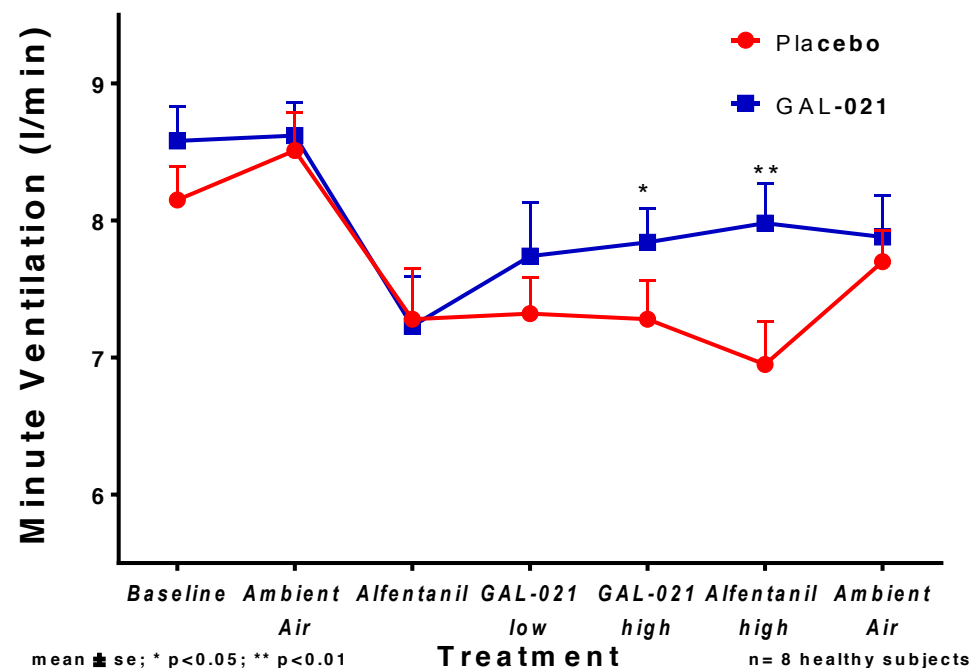


GAL-021 = ENA-001

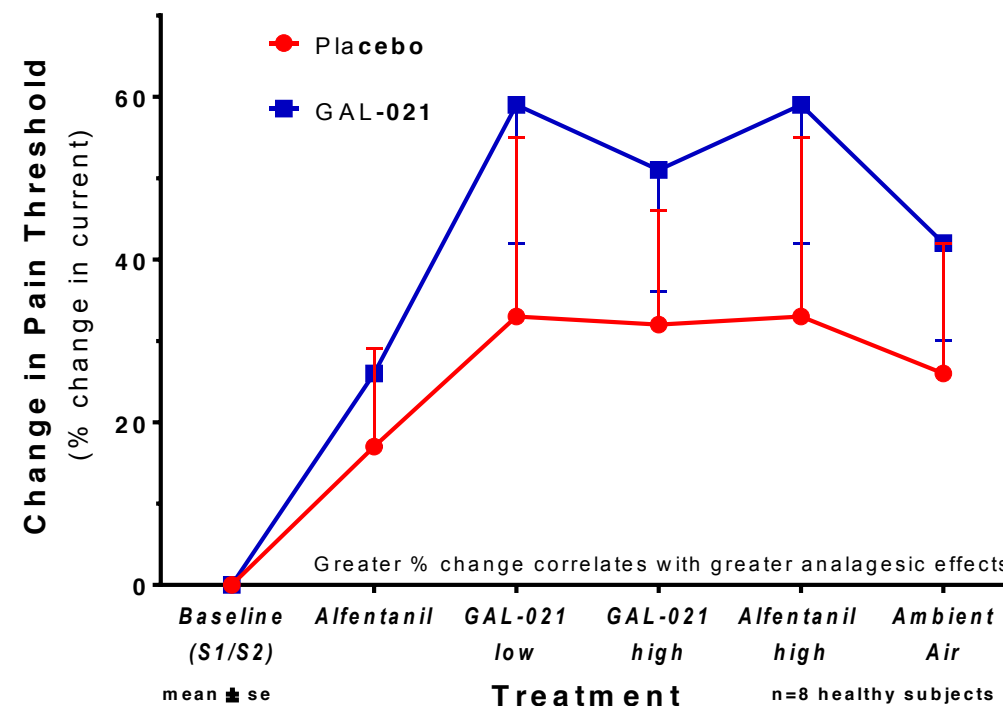


Study 104: part 2 – similar results under ambient air conditions & shows no impact on analgesia

Under Ambient Air Conditions



Did Not Affect Opioid Analgesia



GAL-021 = ENA-001



Study 106: rising multiple dose 5-day 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



ENA-001 Clinical Proof of Efficacy Publication



Two Studies on Reversal of Opioid-induced Respiratory Depression by BK-channel Blocker GAL-021 (ENA-001) in Human Volunteers

Margot Roozekrans, M.D.; Rutger van der Schrier, M.D.; Pieter Okkerse, M.D.; Justin Hay, Ph.D.; James F. McLeod, M.D.; Albert Dahan, M.D., Ph.D.

1. In a double-blind, randomized, placebo-controlled crossover study, ENA-001 stimulated ventilation in male volunteers with alfentanil-induced respiratory depression at a clamped and elevated end-tidal carbon dioxide partial pressure, increasing both tidal volume and respiratory rate
2. ENA-001 also stimulated poikilocapnic ventilation during alfentanil administration, without affecting sedation, antinociception, hemodynamics, or safety parameters

“Pharmacologic ventilator” – Editorial, Joseph F. Cotten, MD, PhD



Pivotal clinical trials will be conducted by a leading world expert on acute respiratory depression

Dr. Albert Dahan

Professor Anesthesiology,
Leiden University Medical Center
The Netherlands

- FDA Advisor/subject matter expert
- Focus on the physiology and pathophysiology of respiratory regulation
- Chairman of the LUMC Institutional Review Board
- Founder and Head of the Anesthesia & Pain Research Unit
- Published over 300 papers in peer-review journals
- MD , VuMC Amsterdam
- PhD, Leiden University

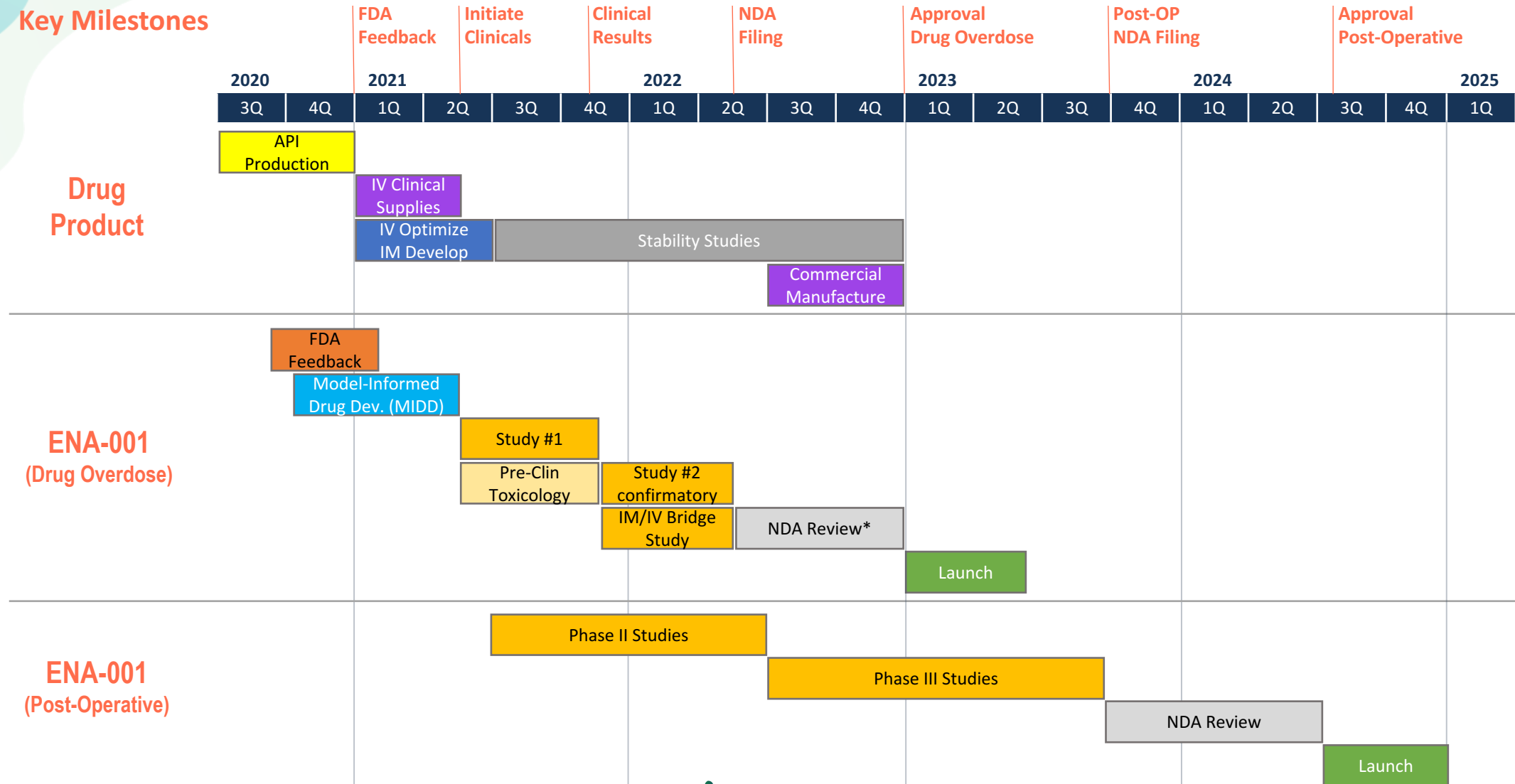
Collaboration with Enalare

- Member of Enalare Scientific Advisory Board
- Developing ENA-001 study designs and will conduct registrational clinical studies
- Enalare sponsoring 2 year postdoctoral fellowship under Dr. Dahan



ENA-001 clear and rapid path to market

Key Milestones



*Opportunity to accelerate review via Breakthrough Therapy and/or Fast Track designation



Significant opportunities across all near-term target markets

Drug Overdose

Net Sales Potential (yr 5)

- \$350M to \$500M+

Market Assumptions

- 7.5M+ unit Naloxone/Narcan Market
- 8% volume CAGR, driven by nasal spray and expanded use in the community setting
- Two new entrants with nasal sprays containing opioid antagonists - naloxone or nalmefene active ingredient

Post-Operative

Net Sales Potential (yr 5)

- \$650M to \$1.5B+

Market Assumptions

- Est. 30M invasive, therapeutic surgeries with anesthesia and standard opioid use
- Additional opportunity in out-patient (ambulatory) setting
- ~1/3rd of patients at high risk of respiratory depression (RD) post-op due to underlying conditions
- 12-17% overall incidence rate of RD

COVID/Resp. Infections

Net Sales Potential (yr 5)

- \$75M to \$250M+

Market

- Assume on-going COVID-19 infections est. 4,000-8,000 new cases/day
- Est. 60% of patients are symptomatic, 15% are hospitalized, 2-3% admitted to ICU, and ~75% then require a ventilator
- On-going incidence of ~200K sepsis/ARDS infections annually (non-COVID-19)



Strong Scientific Advisory Board and support functions

Scientific Advisory Board



Albert Dahan, MD, PhD

World renowned expert in areas of anesthesia and pain and advisor to top regulatory agencies. Founder and Head of Anesthesia & Pain Research Unit at Leiden University. Member of several editorial boards and has published 100s of articles in peer reviewed journals. Leiden University Medical Center, Professor of Anesthesiology



Alexander Kraus, PhD

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 Search & Evaluation at Aquestive Therapeutics.



Eugene Vortsman DO

Practicing emergency medicine specialist with experience treating substance abuse and COVID 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 multiple institutions including Northwell Health, Cornell-Presbyterian Hospital, and University of Medicine and Dentistry of New Jersey



David Battleman, MD

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 pharma/medical device consulting practice within IMS Health. MD, Weill Cornell Medical College, MBA Wharton School of Business, M.Sc. Harvard School of Public Health



Robert Raffa, PhD

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 School of Pharmacy



TJ Gan, MD

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 of Enhanced Recovery (ASER) and dedicated to improving perioperative care through his role in establishing Enhanced Recovery After Surgery (ERAS) programs.

Enalare Support

Alfred Schweikert, PhD, RAC - Regulatory Affairs

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.

Frank Diana, PhD - Operations/CMC

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.



Clinical Research
Organization (CRO)



IP Counsel



NDA Partners
Model Informed
Drug Development

WOLLMUTH MAHER
& DEUTSCH LLP

Corporate Counsel



Healthcare Marketing



Enalare presents a compelling investment opportunity

Poised to fundamentally change clinical practice in the treatment of acute respiratory depression



Significant medical need

- Convergence of health emergencies with commonality of respiratory depression
- Critical need for a safe, agnostic ventilatory stimulant in multiple treatment settings



Robust proof-of-concept

- Positive safety and efficacy results across four human trials
- Extensive pre-clinical platform, including 12 toxicology studies in multiple animal species



Clear & expedient path to market

- Well defined development program with clear endpoints for reversal of respiratory depression
- Initiating registration trials for lead indication – estimate approval in ~ 2 years



Large market opportunities

- Broad medical and health economic benefits driving \$1.5B+ sales potential*
- Novel mechanism-of-action with patent protection through 2031, additional patents pending



Proven top-tier team

- Demonstrated ability to develop and launch blockbuster products with consistent value creation
- Industry leading scientists and advisors



*Enalare internal analysis