



# eva

therapeutics, inc.

株式会社EVAセラピューティクス

eva therapeutics, inc.

April 2023

## Unmet medical needs

- ✓ For severe hypoxemia, the mechanical ventilator and extracorporeal membrane oxygenation (ECMO) are commonly utilized at ICU, while invasiveness, labor and cost are problem
- ✓ Recent pandemic caused supply imbalance, endangering numerous patients' lives at risk

## Core Technology

- ✓ First-in-history "organ" repurposing therapy: enteral ventilation to enable gas exchange
- ✓ EVA101 (first pipeline): A simple enema of liquid oxygen (perfluorocarbon) to prevent or treat the acute deterioration of severe hypoxemia

## R&D strategy

- ✓ EVA101 (device): Japan IND Submission completed in 2022 4Q conducting a clinical trial
- ✓ EVA102 (drug): Initiate pre-oxygenated perfluorocarbon development and US clinical development in 2023 4Q

## EVA101/102 Market Opportunity

- ✓ Japan: USD 100-200 million
- ✓ US&EU5: USD 1-2 billion

## Combination of Young Creative Researchers and Experienced Industry Senior Experts



### Hiromu Ozaki : **Chief Executive Officer**

Ex-CEO of Astellas Pharma Canada, Biogen Japan and Sosei Japan



### Hirofumi Nagai: **Chief Technology Officer**

Ex Head of Takeda Safety Research, Expert in Pharmacology and Toxicology



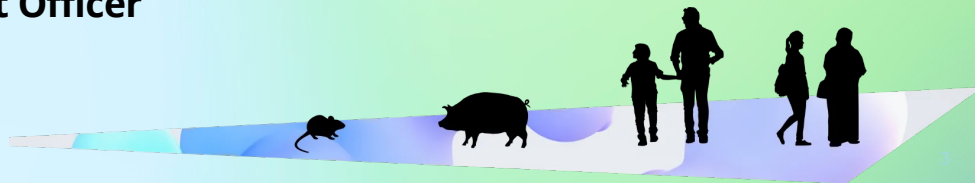
### Yukinori Kanekawa: **Chief Regulatory Officer**

Ex PMDA Lead of Medical Device Evaluation



### Chihiro Yokota: **Chief Development Officer**

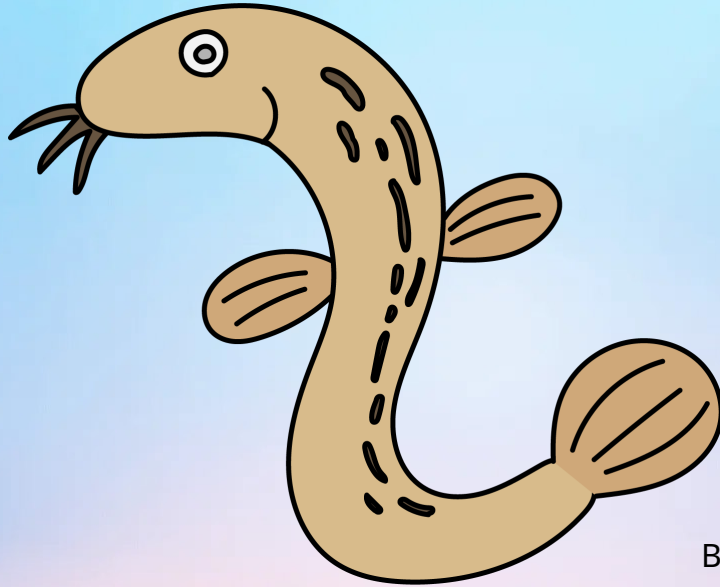
Ex SVP of Development of Astellas



VISION    Unlock New Potential of the Gut

MISSION    Deliver Enteral Ventilation (EVA) Therapeutics

PASSION    Help People, Care for Patients, Cure Diseases



## Accessory breathing mechanisms in fishes

- Esophagus breathers (Crawford, 1971)
- Stomach breathers (Carter & Beadle, 1931)
- Foregut breathers (Nelson et al., 2007)
- Intestinal breathers (Yadav & Singh, 1980)
- Hindgut breathers (McMahon & Burggren, 1987)

Journal of Fish Biology (2014) 84, 554–576 doi:10.1111/jfb.12323.  
Breaking wind to survive: fishes that breathe air with their gut

Translating “gut breathing” mechanism in mammalian

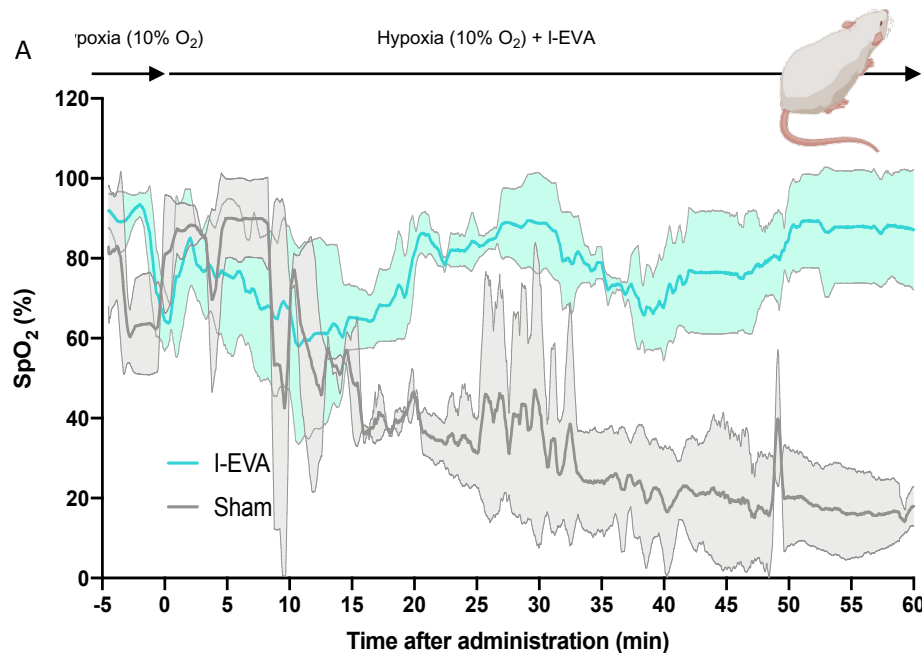
# Our Inspiration: "Perfluorocarbon (Liquid Oxygen)" primes the gut for ventilation

The use of perfluorocarbon (liquid oxygen)



## Inspired by Evangelion

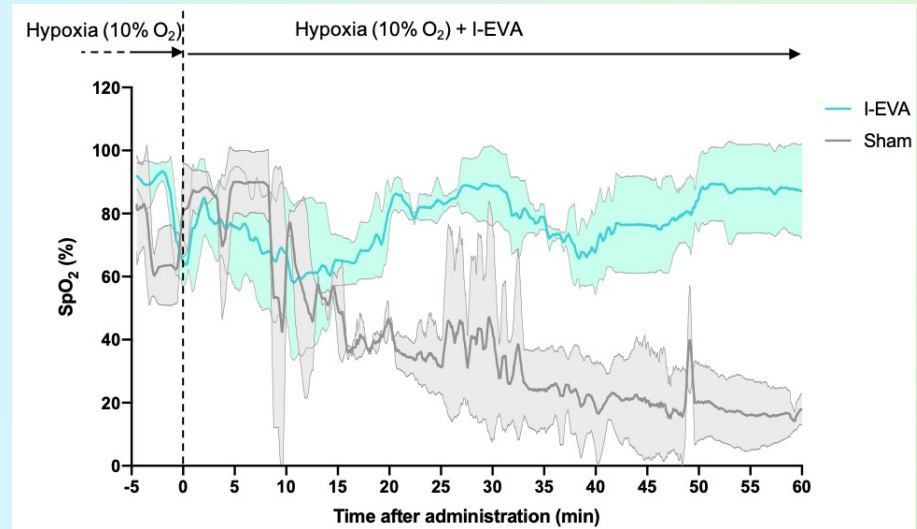
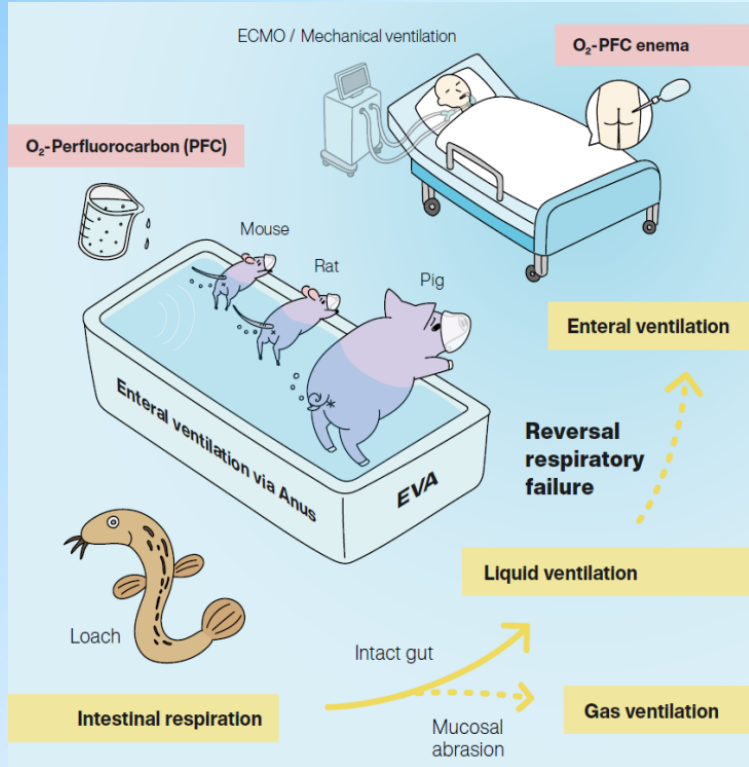
The Entry Plug of an Eva Unit, containing its cockpit, is completely flooded with LCL, and, because it is oxygenated, upon being submerged Eva pilots can "breathe" the liquid (similar to real-life experiments involving liquid breathing).



Enteral ventilation allows for oxygen normalization more than an hour in rodent<sup>6</sup>.

# Proof of Concept of Enteral Ventilation

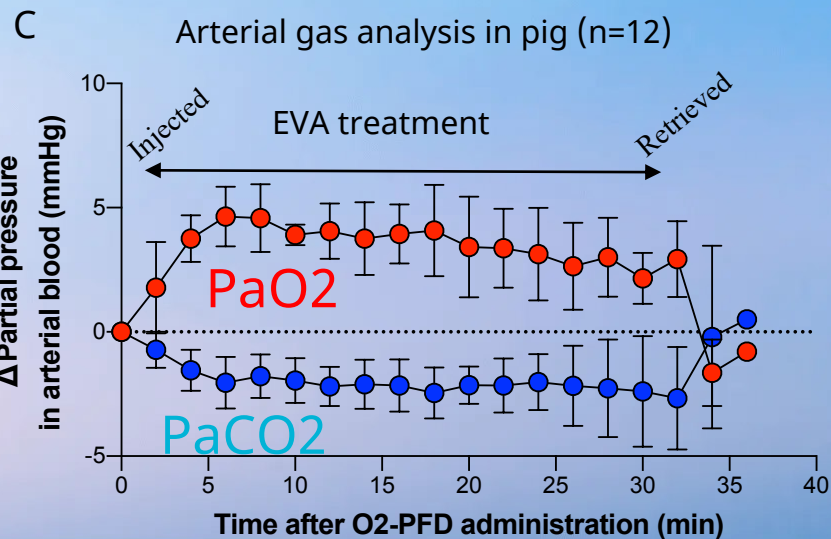
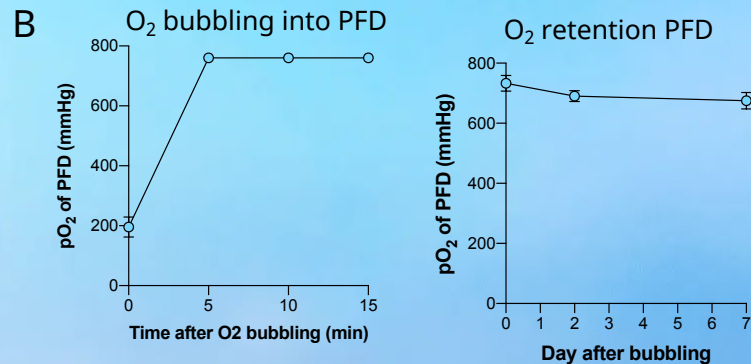
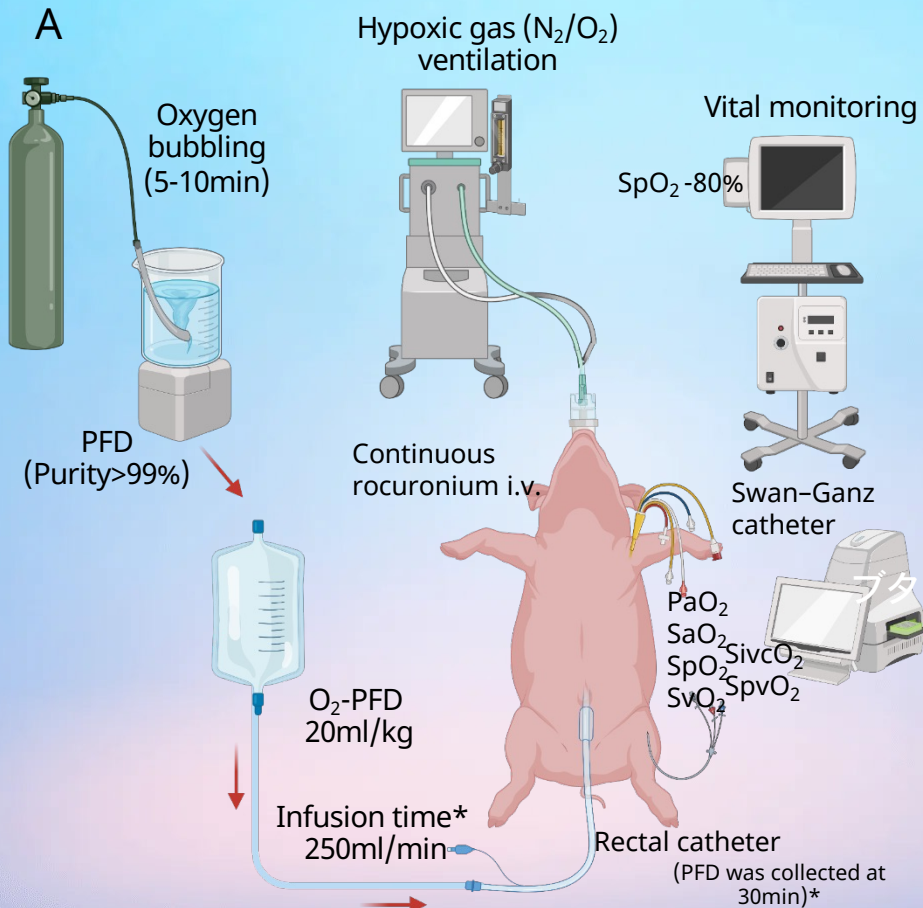
- ✓ Due to the proven safety of perfluorochemicals in clinics, EVA potentially provides an adjunctive means of oxygenation for patients under respiratory distress conditions. *Okabe, et al. Med, 2019*



- The exploitation of intestinal breathing phenomenon in mammalian pre-clinical models.
- Offering an additional route of O<sub>2</sub> administration to patients who are in critical need of immediate respiratory support.

# EVA therapy enabled O<sub>2</sub> increase / CO<sub>2</sub> decrease in large-animal model

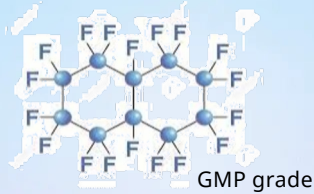
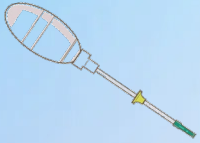
Fujii, et al. *iScience*, 2023



# Our first product EVA101 offers a window to bridge to advanced care

## EVA-101 Kit (Medical Device)

- A) Injection bag      B) PFD(perfluorodecalin)



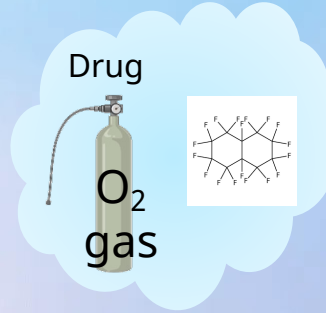
- C) Other components

- Bubbling cannula, Filter, Needle, etc

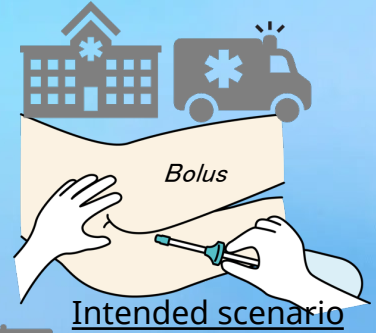
- D) Instruction Materials

- Bubbling, Collection and Disposal protocols

## Oxygen bubbling



After bubbling, O<sub>2</sub> conc  
can be sustained over  
6months at least



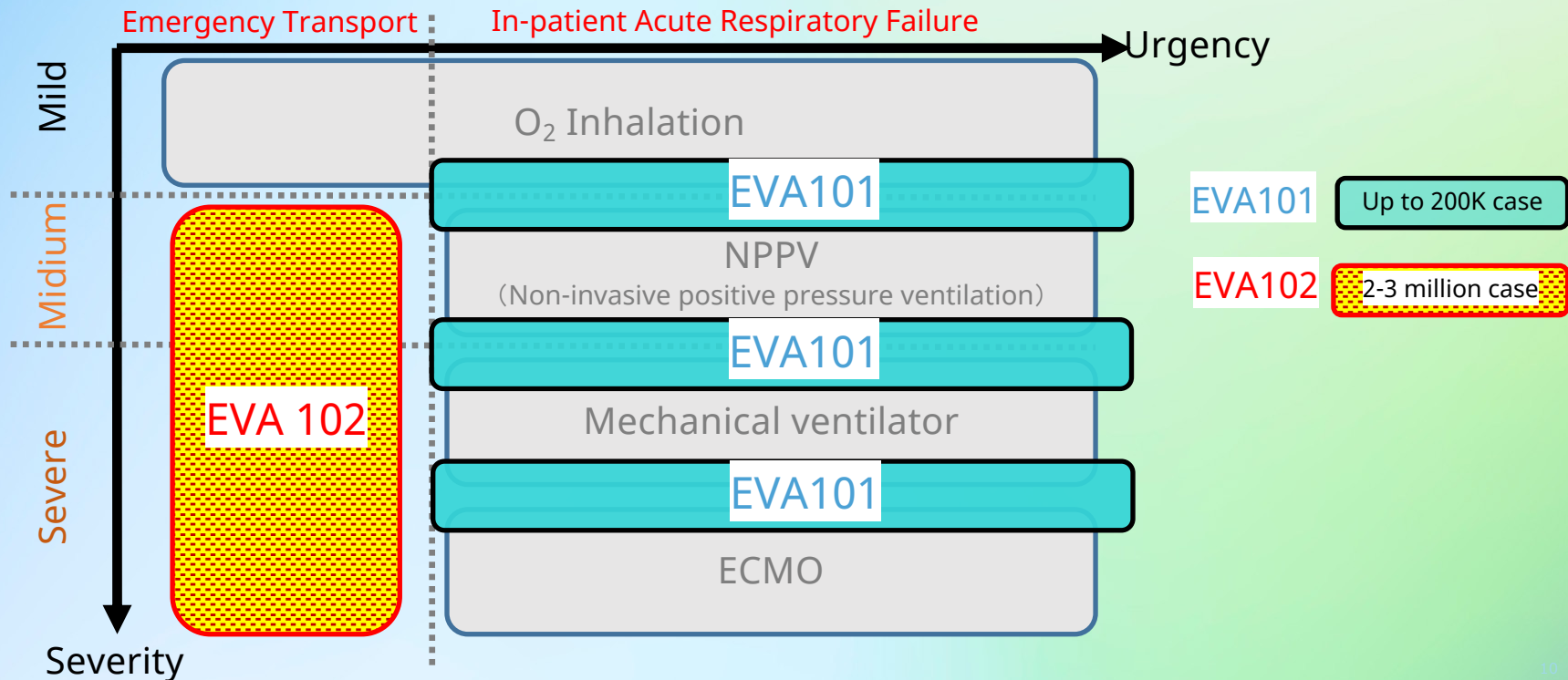
Bridge to advanced  
medical care during  
medical transport

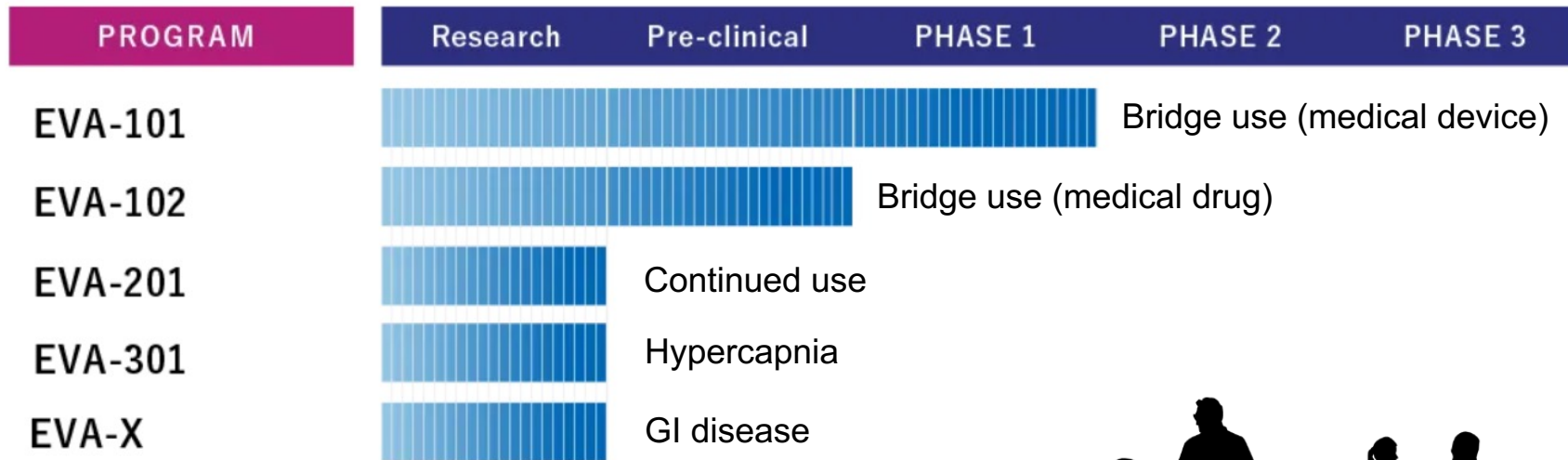
Intubation difficulty  
or denial cases to  
provide temporal  
support

Preparation to NPPV,  
MV and ECMO

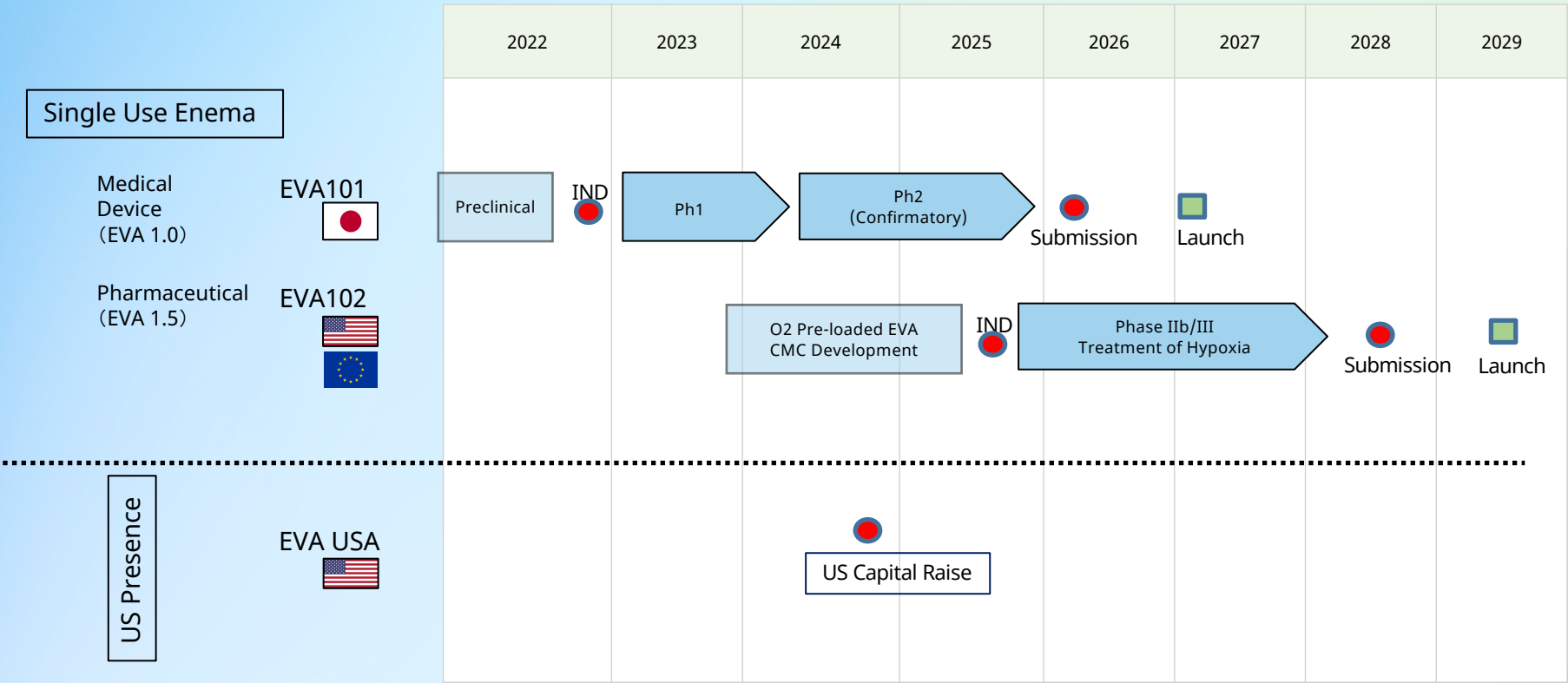
# EVA101&102 will bridge emergency patients to advanced care

Target : 3 million Acute Respiratory Failure cases a year in US





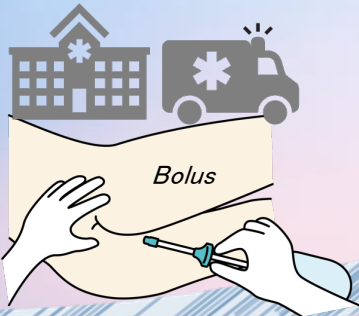
# EVA Clinical Development Timeline



# EVA Technology - Clinical Narrative

## Stage 1

**EVA101**  
Single Use  
EVA 1.0 for Japan



## Stage 2

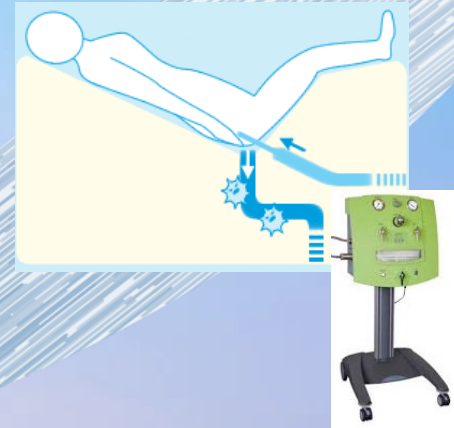
**EVA102**  
O2 pre-loaded Ready to  
Use Enema  
EVA 1.5 global



Bridge to advanced  
medical care during  
medical transport

## Stage 3

**EVA201**  
Continuous Use  
EVA 2.0 global



TMDU

Translational research

Cincinnati Children's

Organoid research

Drug development

Our Scientific Team

Street Medical research

T-CiRA

YCU-CDC

THANK YOU!

