



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



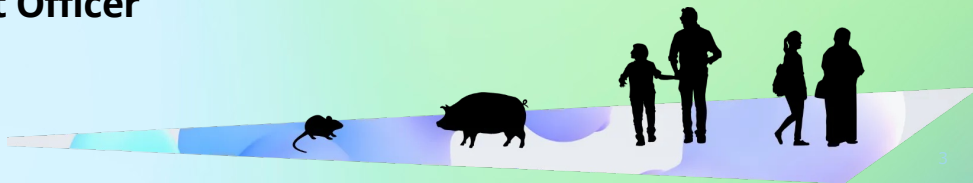
Hirofumi Nagai: **Chief Technology Officer**
Ex Head of Takeda Safety Research, Expert in Pharmacology and Toxicology



Yukinori Kanekawa: **Chief Regulatory Officer**
Ex PMDA Lead of Medical Device Evaluation



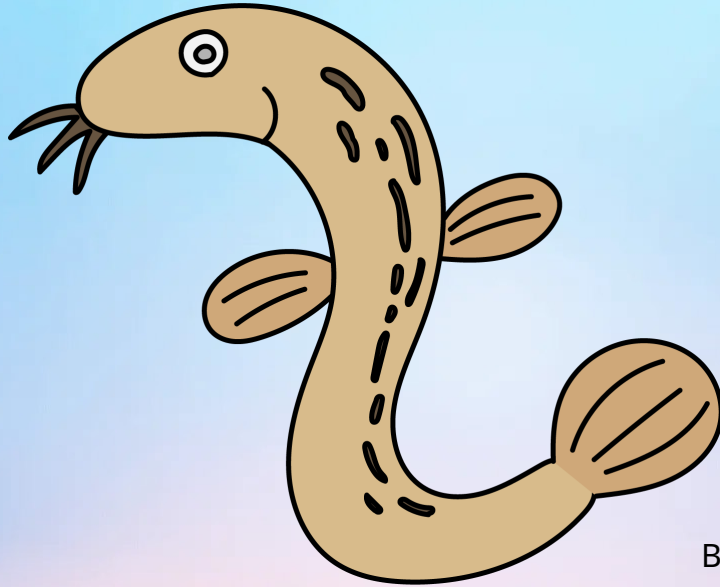
Chihiro Yokota: **Chief Development Officer**
Ex SVP of Development of Astellas



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

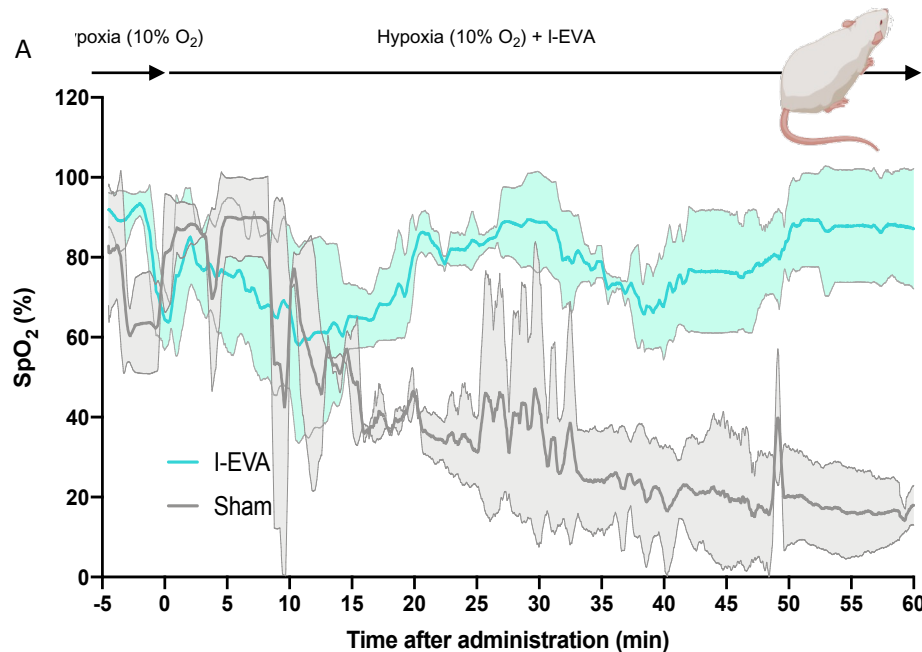
Our Inspiration: "Perfluorocarbon (Liquid Oxygen)" primes the gut for ventilation

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).

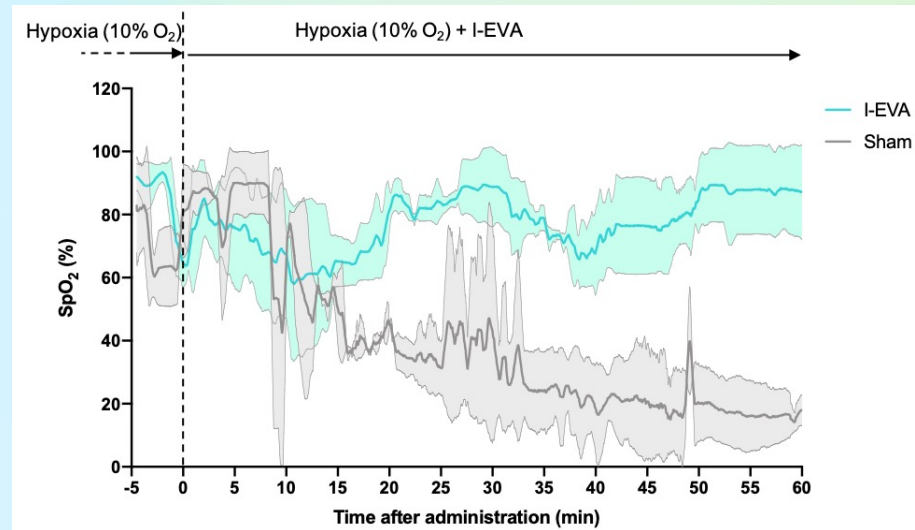
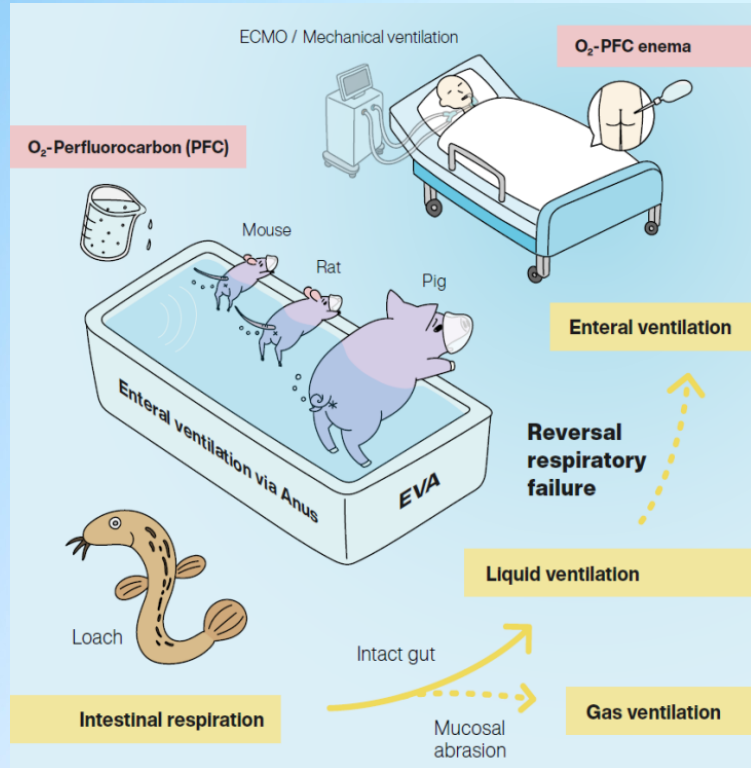


Enteral ventilation allows for oxygen normalization more than an hour in rodent⁶.

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.

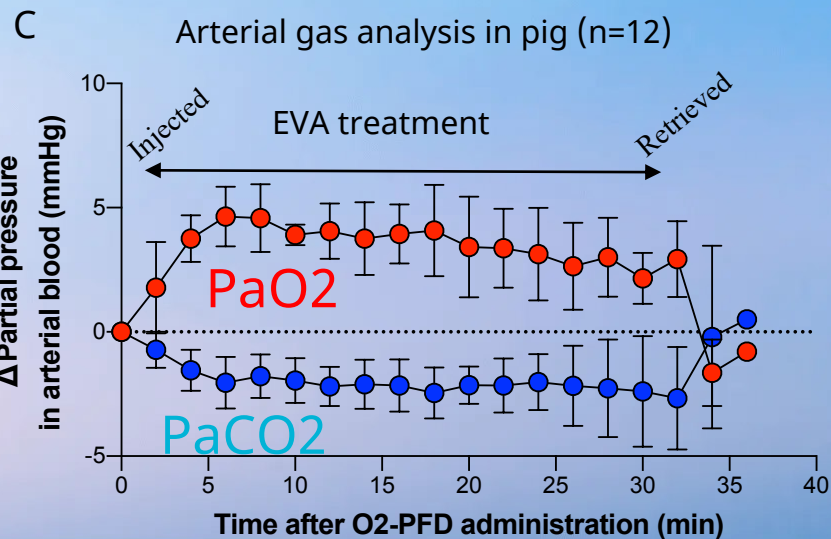
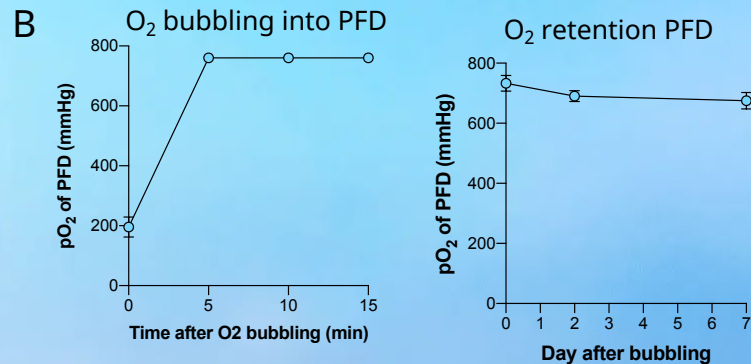
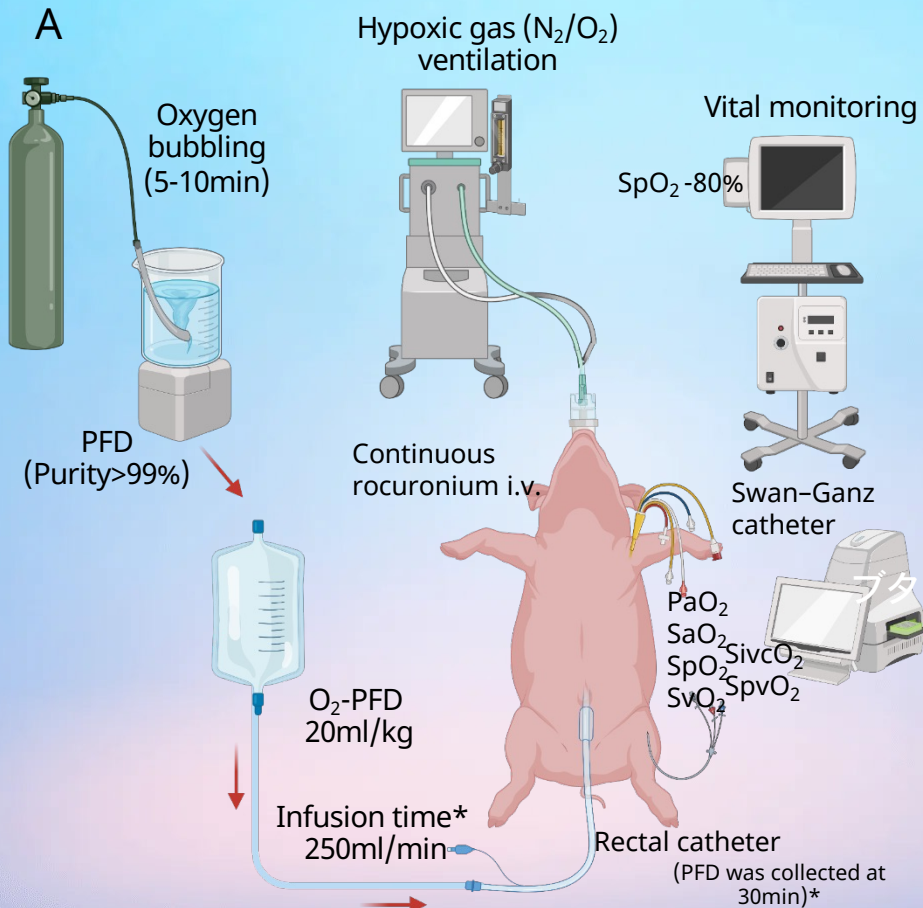
Okabe, et al. Med, 2019



- The exploitation of intestinal breathing phenomenon in mammalian pre-clinical models.
- Offering an additional route of O₂ administration to patients who are in critical need of immediate respiratory support.

EVA therapy enabled O₂ increase / CO₂ decrease in large-animal model

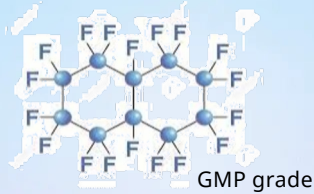
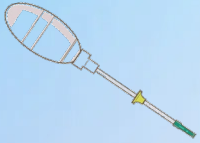
Fujii, et al. *iScience*, 2023



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

EVA-101 Kit (Medical Device)

- A) Injection bag B) PFD(perfluorodecalin)



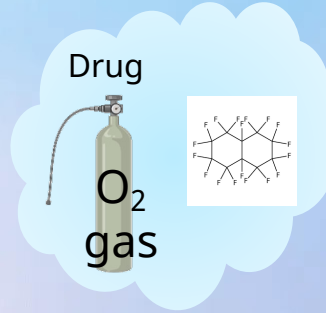
- C) Other components

- Bubbling cannula, Filter, Needle, etc

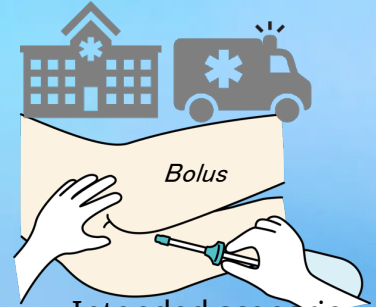
- D) Instruction Materials

- Bubbling, Collection and Disposal protocols

Oxygen bubbling



After bubbling, O₂ conc
can be sustained over
6months at least



Intended scenario



Bridge to advanced
medical care during
medical transport



Intubation difficulty
or denial cases to
provide temporal
support

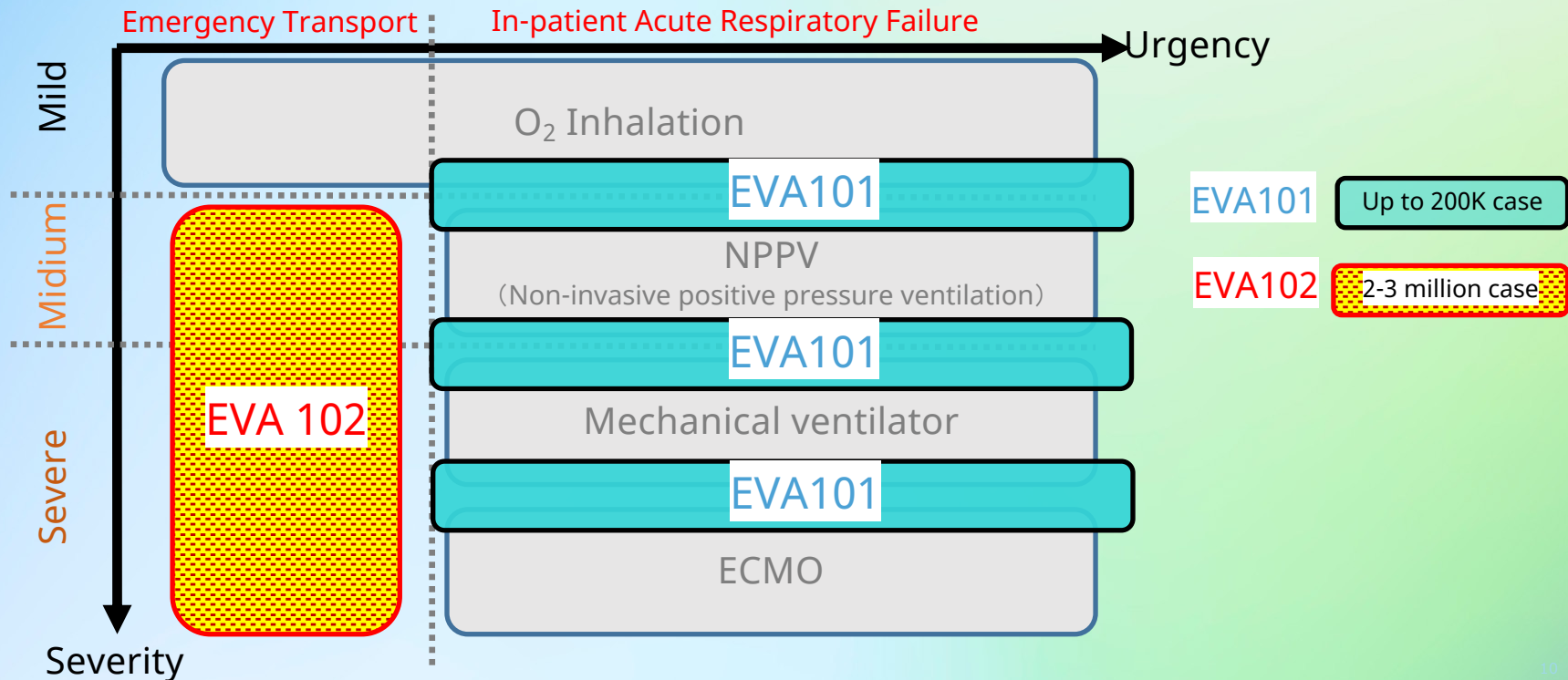


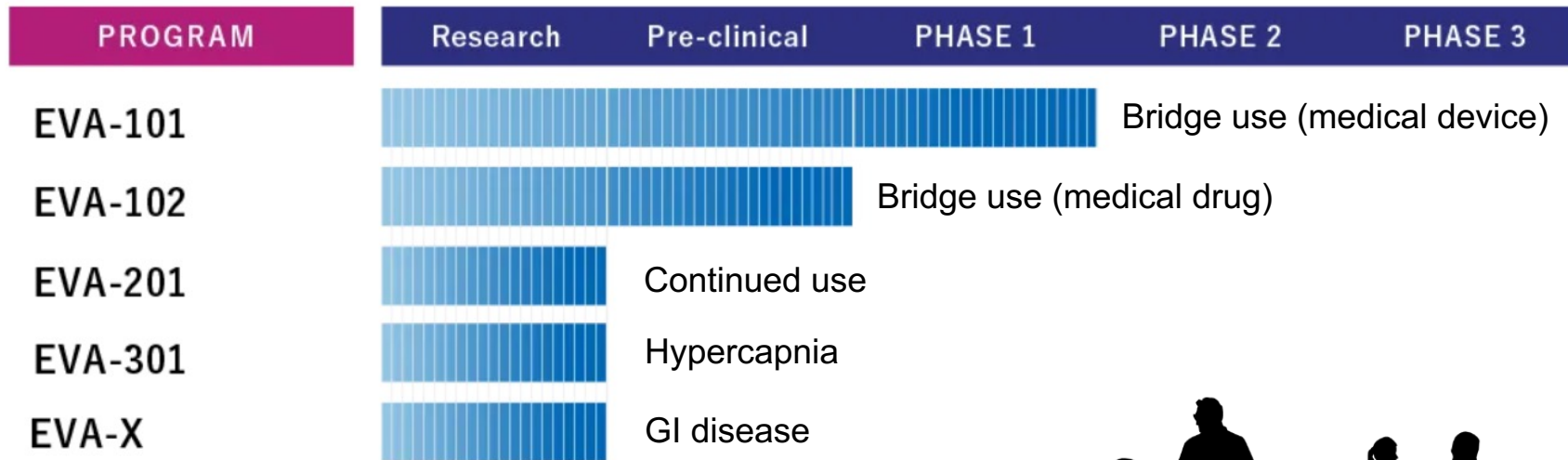
Preparation to NPPV,
MV and ECMO



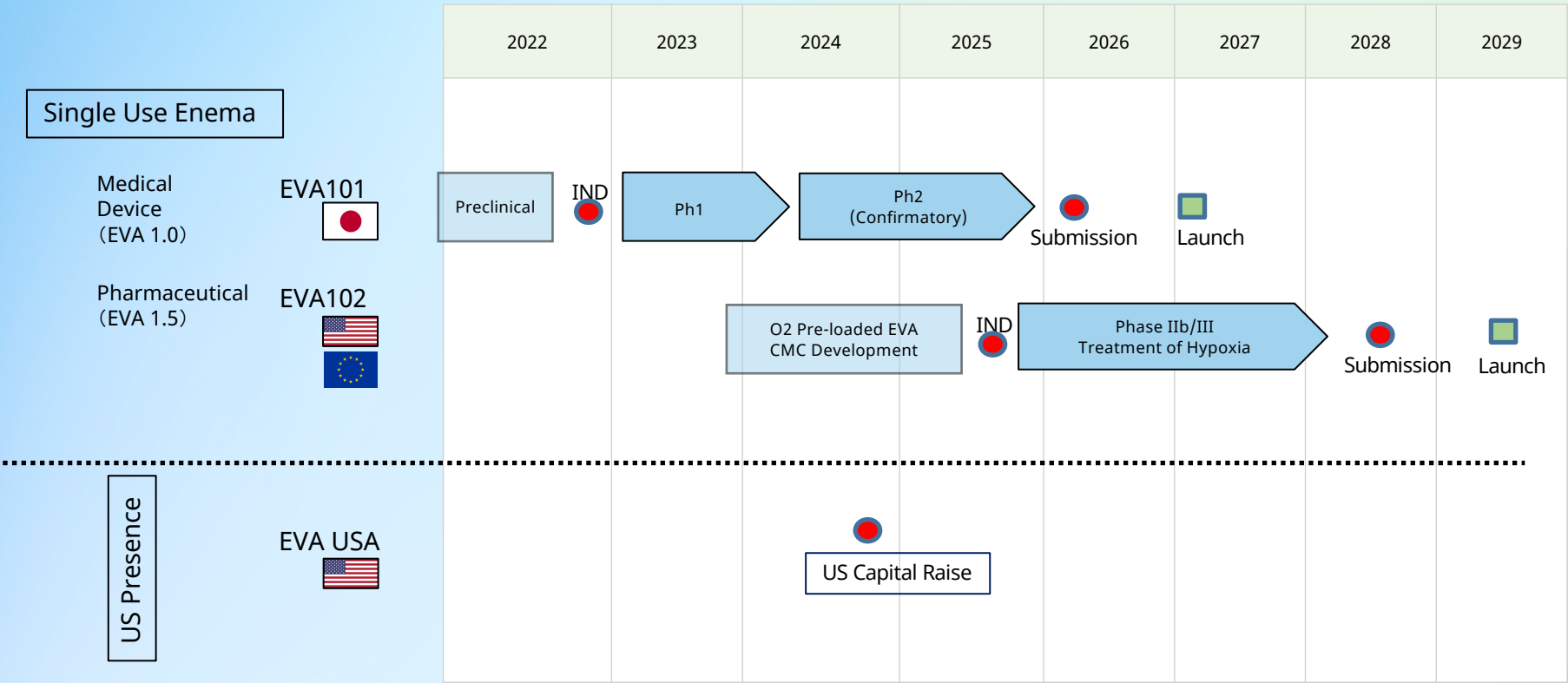
EVA101&102 will bridge emergency patients to advanced care

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





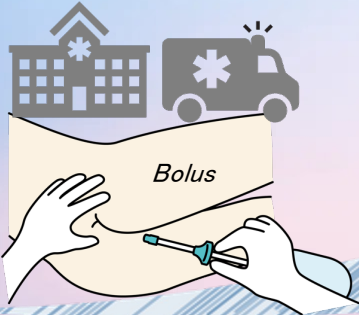
EVA Clinical Development Timeline



EVA Technology - Clinical Narrative

Stage 1

EVA101
Single Use
EVA 1.0 for Japan



Stage 2

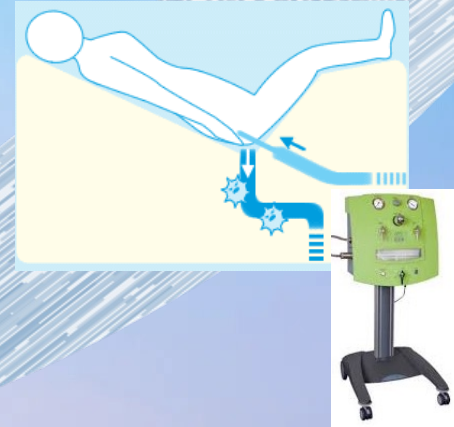
EVA102
O2 pre-loaded Ready to
Use Enema
EVA 1.5 global



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!

