Can Spraying be Precise?

Introducing **SPRACISE** – a Novel Platform for Localized Deep Nasal Delivery

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Clexio at a Glance

Multi-Asset Clinical Pipeline

- ✓ 4 clinical stage programs
- ✓ Lead asset completed Phase 2
- ✓ Advancing internally discovered preclinical pipeline
- ✓ 31 patent families, 22 granted in US

Focus on CNS and Psychiatry

- ✓ Targeting significant unmet needs
- ✓ Developing Drug and Drug-Device Combination Products

Using validated MOAs

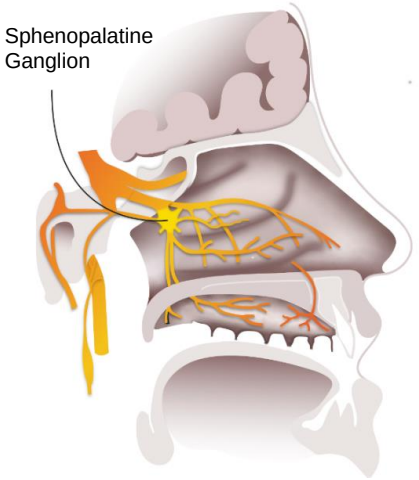
- ✓ Focus on validated Mechanism of Actions
- ✓ De-risked clinical development pathways

Localized Deep Nasal Delivery offers potential key advantages for applications requiring targeted action, with the aim of *increasing efficacy* vs traditional nasal sprays

- Traditional Nasal Sprays dispense drugs broadly in the entire nasal cavity without focusing on a particular target
  - Broad dispensation and low specificity
  - High systemic exposure and increased risk of adverse effects
- Localized nasal delivery offers several key value points, making it an attractive option for drug delivery in certain therapeutic applications:
  - Enhanced targeting specificity and reduced systemic exposure
  - Higher local drug concentrations
  - Rapid onset of action
  - Minimized first-pass metabolism
  - Reduced Interactions with other medications
- In recent years, specialized nozzles and propellant mechanisms have been developed to reach specific regions in the nasal cavity. However, most are focused on anterior targets and not deep posterior ones

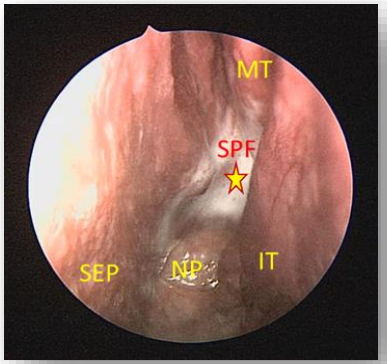
Case Study: SPG-Targeted Therapeutics for *"the worst pain known to man"*

- **Cluster Headache** is a neurological disorder characterized by extremely severe recurrent headaches on one side of the head
- **High Unmet Need**: Patients currently have limited treatment options to prevent or stop attacks
- **SPG block** with local anesthetic is a clinically validated approach, targeting a specific nerve pathway at the **Sphenopalatine Ganglion (SPG),** a large extracranial parasympathetic ganglion involved in activation of the trigemino-vascular system
- Current SPG block techniques are intended for administration by a healthcare professional and their success is highly operator-dependent

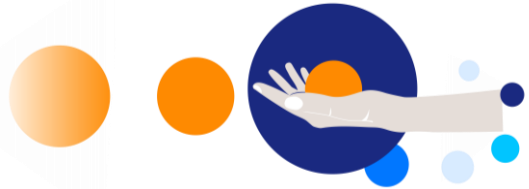


SPRACISE: Is being developed as the device component of a first-of-its-kind combination product to achieve rapid relief of Cluster Headache attacks, by *self-administration*

- **SPRACISE*** aims to place the treatment in the hands of the patients such that it is conveniently portable and easy to use



- Prototype was tested successfully in **in-vitro & ex-vivo models**, confirming precise dosing to the target area in the tested models
- **3 Human Factor Studies** in Cluster Headache patients were performed, demonstrating usability and self administration
- Initiated **First-in-Human** Clinical Study



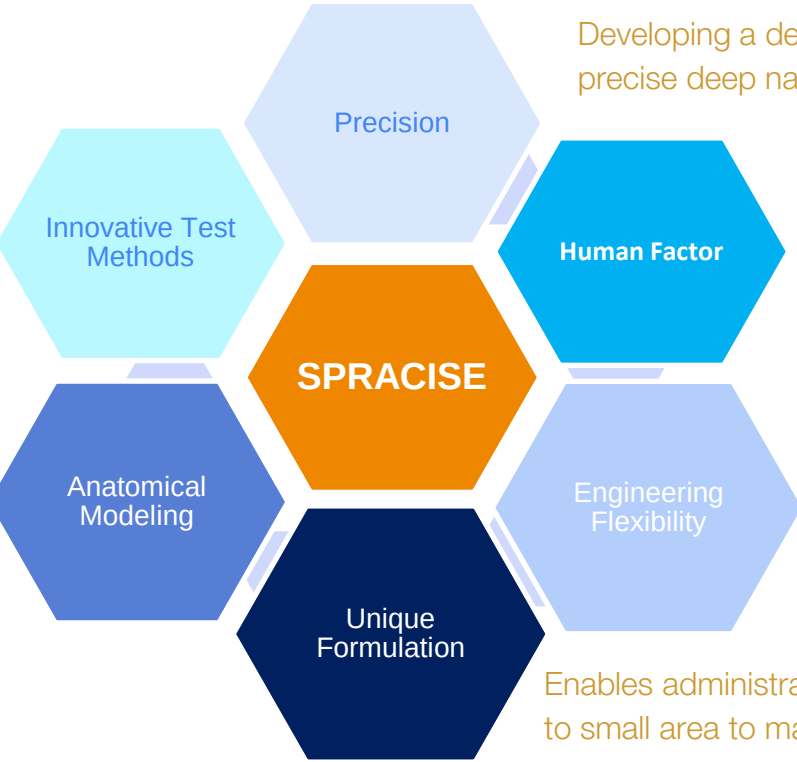
**SPRACISE is the device component of a new investigational drug-device combination that has not been approved for commercial distribution.*

Addressing challenges involves a mix of innovative formulations, device engineering, and carefully considering user needs

- **Challenges**
  - Anatomical Variability between individuals (and within individuals)
  - Mucociliary clearance, swallowing, sneezing, dripping
  - Container Closure System compatibility
  - Specific delivery pattern and profile to achieve accuracy and focus
  - Patient compliance and competency during attack.

- **Success Strategies**
  - Computational Models to determine optimal Device Design Inputs
  - Physical properties of the Drug formulation, enhancing retention time and absorption
  - Constant collaboration between drug and device; optimizing tolerances
  - Controlling flow force and nozzle geometrical design; empirical testing
  - Human Factors of Self-Administration in the absence of a familiar mental model

Clexio's Expertise in Deep Nasal Localized Applications



Developing a device that targets precise deep nasal application

Formative studies in target patient population: confirming usability and providing valuable use data

Can be adjusted to target different API, doses and areas in the nasal cavity

Enables administration of high volume to small area to maximize absorption

Harnessing Machine Learning tools to overcome variability in patients' anatomy

In Vitro and Ex Vivo studies to verify application accuracy

Summary: *Localized deep nasal delivery* is an attractive option for a range of medical conditions

- *Clexio has developed a **technology to deliver precise quantities of drugs to specific locations of the nasal cavity**. The device is small, portable, easy and convenient for use and suitable for self administration. The device could deliver various formulations, with a desired spray plume geometry.*
- ***SPRACISE** first prototype was developed to target the Sphenopalatine Foramen in the nasal cavity, to abort Cluster Headache pain. **Currently tested in a Phase 1b study***
- ***Other potential utilizations:***
  - **Vaccines**: using SPRACISE to provoke efficient mucosal and systemic immune response by targeted delivery to the **NALT** (Nasal Associated Lymphoid Tissue) (Fig 1).
  - **Crossing the BBB**: using SPRACISE to enhance drug penetration to the Brain through the olfactory region. Potential utilization: meningitis, neurology, nucleic acid based therapies, others

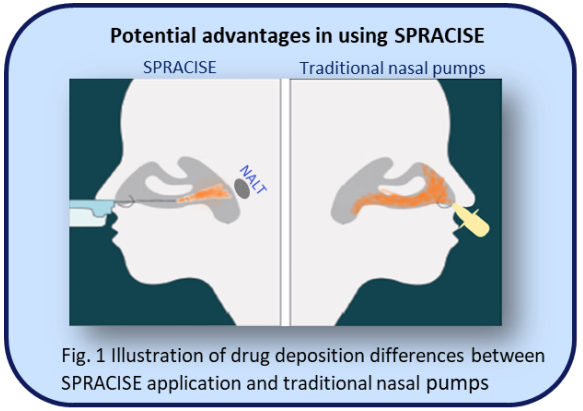


Fig. 1 Illustration of drug deposition differences between SPRACISE application and traditional nasal pumps

THANK YOU!

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