



# OptiNose

## The Key to Successful Nasal Drug Delivery

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**OptiNose**  
DRUG DELIVERY DEVICES  
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- Company Update
- OptiNose Delivery Technology
- The Founder's challenges



## Company Update

- OptiNose AS is a privately owned company founded in October 2000
- Portfolio of patents and patent applications broadly securing its technology
  - Core patent granted in US and Europe
  - Follow on patents claiming aspects of technology and product focussed applications
- Shareholders: Founders, Inspire AS, Andromeda-Fund BV, WFD Ventures LLC
- Latest fund-raising round completed December '05



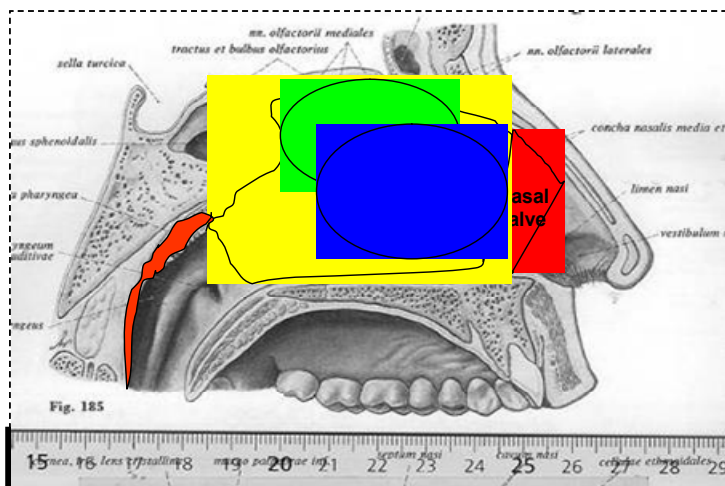
# Nasal delivery offers significant advantages for treating many diseases

	Features & advantages	Therapeutic fields of interest	Classes of substances & drugs
<b>Topical delivery</b>	<ul style="list-style-type: none"> <li>Target directly diseased organ/site of interest</li> <li>Avoid systemic side-effects</li> <li>Reduced dose</li> </ul>	<ul style="list-style-type: none"> <li>Allergic rhinitis</li> <li>Non-allergic rhinitis</li> <li>Rhinosinusitis</li> <li>Nasal polyposis</li> <li>Acute sinusitis</li> <li>Common cold</li> <li>Vaccination</li> </ul>	<ul style="list-style-type: none"> <li>Topical steroids</li> <li>Antihistamines</li> <li>Immuno-modulators</li> <li>Decongestants</li> <li>Vaccines</li> </ul>
	Features & advantages	Therapeutic fields of interest	Classes of substances & drugs
<b>Systemic delivery</b>	<ul style="list-style-type: none"> <li>Non-invasive/Self-medication - replace injection</li> <li>Improved patient compliance</li> <li>Thin mucosa and high blood flow</li> <li>Fast absorption and fast onset of action</li> <li>Avoid/reduce GI-side effects</li> <li>Avoid first pass effect in liver</li> <li>Reduce enzymatic degradation</li> <li>Improved PK profile</li> <li>Potential combination with N2B action</li> </ul>	<ul style="list-style-type: none"> <li>Analgesics (fast action)</li> <li>Migraine &amp; headache (fast action)</li> <li>Insomnia &amp; sedation (fast action)</li> <li>Obesity</li> <li>Diabetes I &amp; II</li> <li>Other endocrine diseases</li> </ul>	<ul style="list-style-type: none"> <li>Polar drugs with poor GI-absorption</li> <li>Proteins &amp; peptides degraded in GI-tract</li> <li>Hydrophilic &amp; high molecular weight peptides</li> <li>Small molecules with intended fast action</li> </ul>
	Features & advantages	Therapeutic fields of interest	Classes of substances & drugs
<b>Nose-to-Brain delivery (N2B)</b>	<ul style="list-style-type: none"> <li>Absence of intact BBB in olfactory region</li> <li>Potential transport along olfactory nerves</li> <li>Potential transport along trigeminal nerves</li> <li>Absorption via veins draining to sinus cavernous</li> <li>Reduce systemic and GI side effects</li> <li>Improved CNS effect with lower systemic BA</li> </ul>	<ul style="list-style-type: none"> <li>Analgesics (fast action)</li> <li>Migraine &amp; headache (fast action)</li> <li>Insomnia &amp; sedation (fast action)</li> <li>Alzheimer's &amp; Parkinson's</li> <li>Neurodegenerative diseases</li> <li>Obesity</li> <li>Other endocrine diseases</li> </ul>	<ul style="list-style-type: none"> <li>Neuroactive polar drugs with poor GI-absorption</li> <li>Neuroactive proteins &amp; peptides</li> <li>Neuroactive small molecules with fast action</li> </ul>

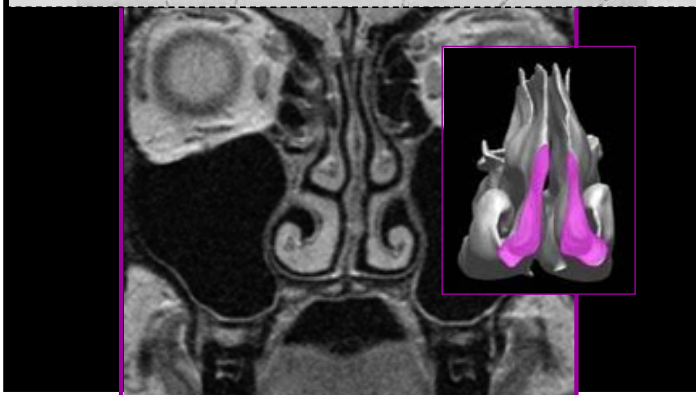


# Drug delivery through the nose

- **Topical delivery**
- **Systemic delivery**
- **Nose-to-Brain delivery**
- **Vaccine delivery**



- Anterior third of nose lined by skin-like epithelium. Not true mucosal surface.
- True nasal mucosa lies beyond nasal valve.
- The thin nasal mucosa and dense network of blood vessels beneath create potential for rapid drug absorption.
- Nasal absorption limits the problem with degradation of drugs in the stomach and in the liver





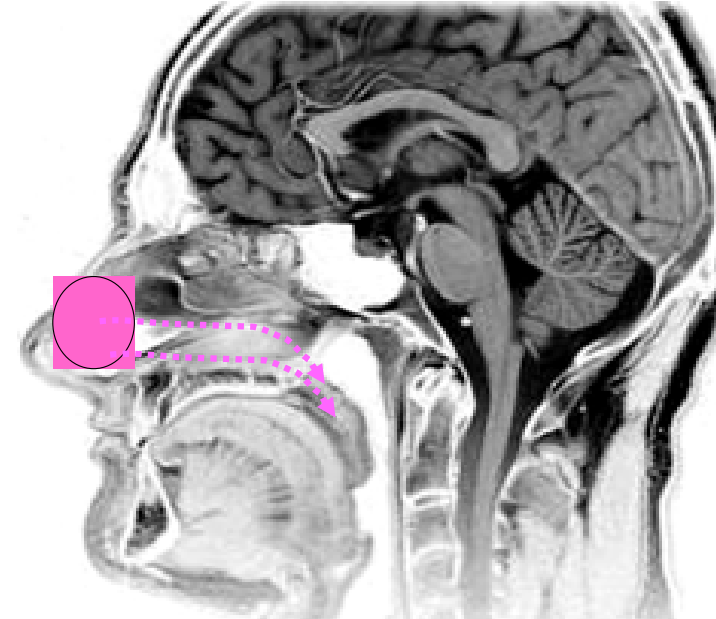
# The potential of nasal delivery has not been realized due to technology limitations

## Review of the literature

(Spray pumps, pMDI's, Powder inhalers, drops)

Traditional nasal delivery methods deliver most of the dose (50-100%) anterior to the nasal valve.

The fraction bypassing the nasal valve passes mainly along the floor of the nose to be swallowed.



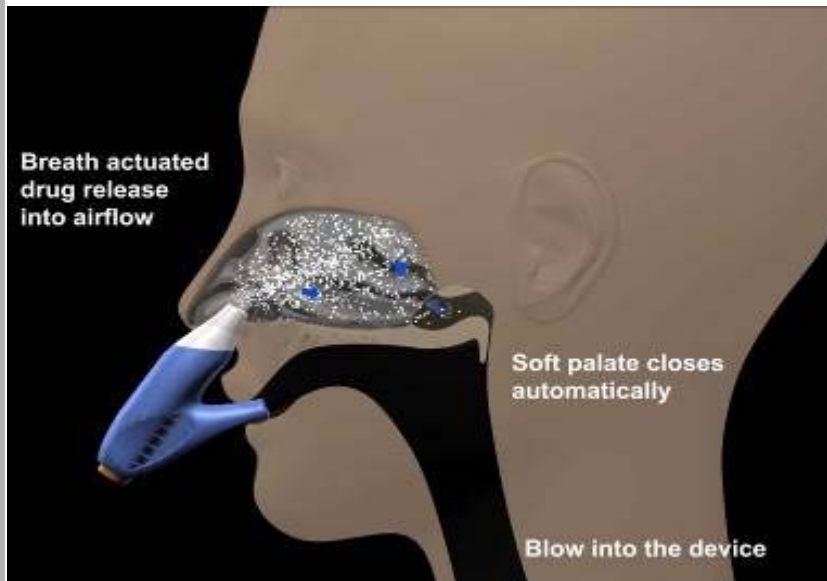
## Conclusion:

**Existing delivery methods are suboptimal for nasal drug delivery targeting sites beyond the nasal valve**

The assessment of topical nasal drug distribution. Aggrawal R et al. Clin Otolaryngol. 2004, 29, 201-205 ■



# OptiNose's Delivery Technology Overcomes Nasal Delivery Challenges - How it Works



## Breath actuated bi-directional delivery

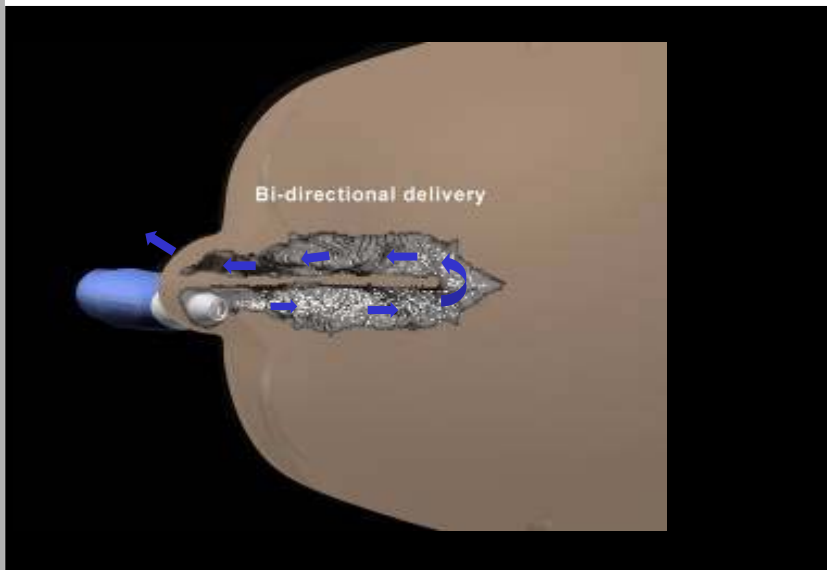
While exhaling into the device, the soft palate automatically closes off the nasal cavity completely ...

... the breath enters one nostril through a sealing nozzle

... and actuates the release of particles into the airflow - carrying particles beyond the nasal valve to target sites

... the air flow passes through the communication posterior to the nasal septum

... and exits through the other nasal passage in the opposite direction





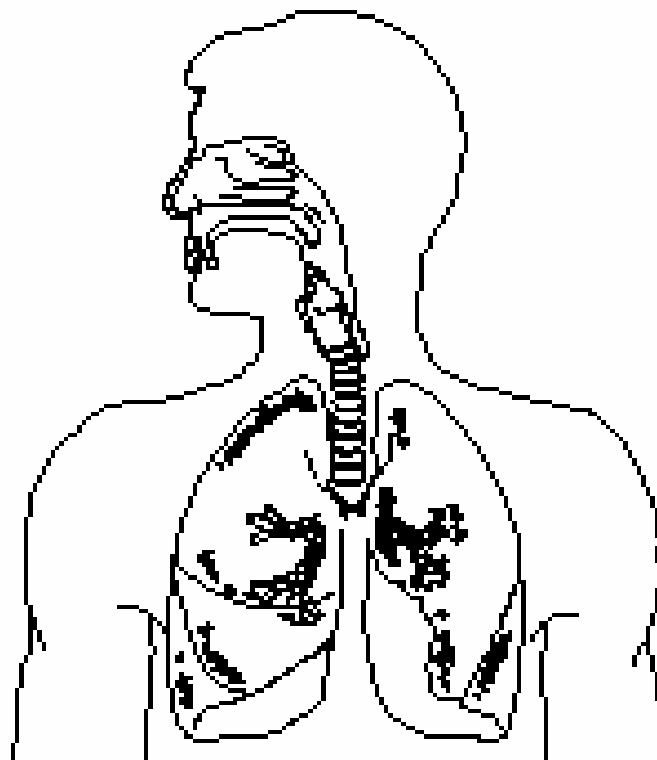
# Minimal Risk of Inhalation to Lungs

## Nasal inhalation



**27% of dose  
in lungs**

## Study in 16 subjects



**Inhalation of 2-5  
micron particles from  
PARI Nebulizer**

## Bi-dir. delivery



**No radioactivity  
above backgr.**

*Djupesland PG et al. JAM 2004; 17(3); 249-59.*





## OptiNose Device Achieves >90% *in vivo* Deposition Beyond the Nasal Valve with Excellent Reproducibility

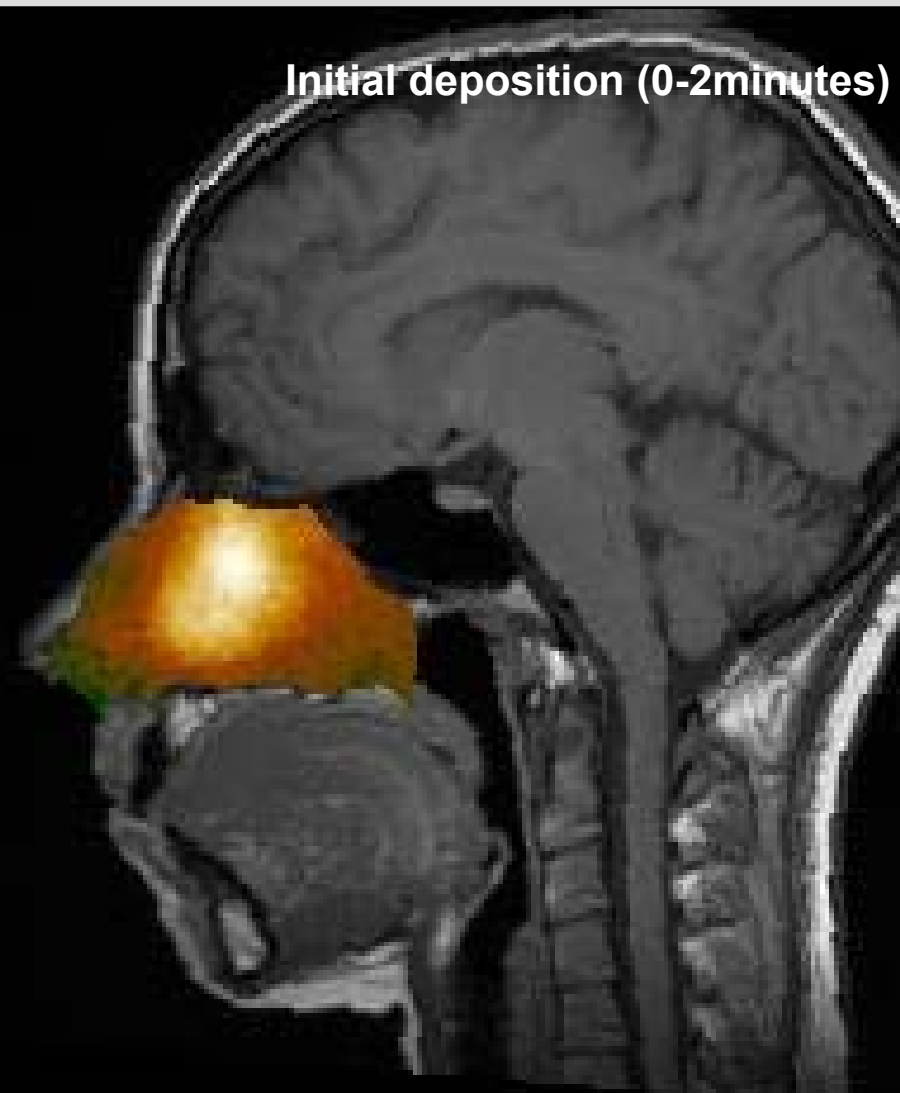
(average in 7 subjects)

### OptiNose Delivery Device

- >90% of emitted dose is deposited beyond the nasal valve
- >70% of emitted dose deposited in the upper posterior 2/3 of the nasal cavity
- High reproducibility of deposition beyond the nasal valve
- Prevents lung deposition
- Fulfils the ideal requirements



Initial deposition (0-2minutes)





# OptiNose Liquid and Powder Delivery Devices

## Multi-dose Liquid Delivery Device



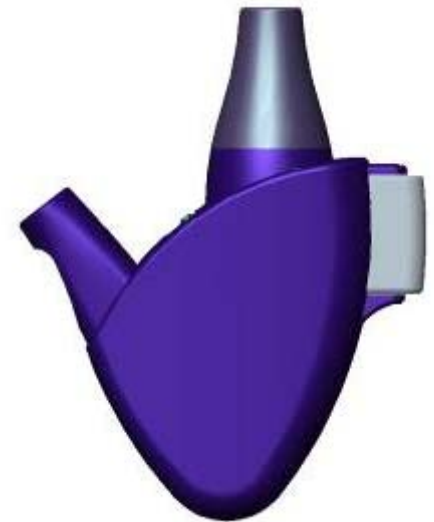
**Liquid:** Standard spray pump inside.

**Powder:** Disposable unit-doses with a reusable device body: the drug is contained within a capsule that is pierced before delivery of the dose.

### Common features

- Breath actuated, bi-directional delivery
- Incorporates proven principles
- Incorporates components from existing device technologies
- Devices moulded from single cavity hardened steel tools for clinical trials

## Multi-dose Powder Delivery Device





# The Founder's challenges

- The business plan
- Resources (People & money)
- Protecting Intellectual Property
- Developing products



# The Business Plan

## - From Idea to Product

- Follow a good "recipee"
- Access Market Research Data
- Get advise from industry experts
- Focus on how to create value-find out what is unique with your idea and build your product on these attributes
- Review the business plan regularly – it is a living document
- Think very clearly the short term plan, because the long term plan may change due to factors you cannot control



## OptiNose - Business Model focused on creating value

- **Develop combination products and out-license after proof of concept to build shareholder value**

*OptiNose to develop in-house **drug/device combination products** for selected high value marketplace opportunities where OptiNose creates visible competitive advantage*

- **Out-license device IP**

*Partner with pharmaceutical companies on specific compounds in return for development costs, milestones and royalties*



# Why product development and not pure drug delivery.....

- Illustrate the areas where the technology creates advantage
- Control own destiny
- Advance products towards the marketplace
- Enhance deal terms by moving further up the value chain
- Develop the device platform



## Resources –The Team

- Most important in the beginning and all the way: commitment –high degree of motivation and belief in the product
- Identify necessary key resources
- Add industry expertise
- Work for team motivation and be determined, patient and focussed



# Human Resources – make the team play work

Have values & develop a basis of trust

- Clear objectives & milestones
  - Business plan
- Efficient communication
  - Bring closer different backgrounds and cultures
  - Management of expectations
- Ensure information flow
  - “Everyone on the same page”
- Take care of the people
  - Balance individual interests with company interests
- Handle conflicts
  - Encourage openness and no hidden agendas
  - Corporate culture





## Resources –Money

- Find all possible grant sources & write good applications- be careful about IP clauses
- Get good advise on your valuation and fundraising
- It is never too early to start with the next phase of fundraising
- If possible, choose the investor you like
- Nourish your investor relationship



# Nourish your investor relationships

Create a basis of mutual trust for a long term mutually beneficial co-operation

- Inform on important achievements
  - Create relationship
  - Keep interest living
- Inform on adverse events and suggest solutions
  - Demonstrate control of the situation
  - Give the real picture
- Get advise and support from stakeholders
  - Ask the view of independent directors, your executives, your advisers
- Use written agreements
  - Legal contracts are there to be respected-comply and require compliance



# Intellectual Property Protection

- This is your core asset
- It is crucial to get a good patent attorney with expertise in your area
- File new patents- ring fence
- Never disclose confidential information without CDA (prefer one-way, use a law system that you know)
- Almost never disclose information that is not in the public domain, even under confidentiality
- Defense: freedom to operate searches



# OptiNose -List of post placement challenges & tasks

- Complete recruitment of competent resources
- Governance structures
- Set up a clinical program for 2 drug & device combinations
- Select Clinical Research organisations
- Select clinical trial sites
- Prepare applications to ethics committees and authorities
- Develop two reliable devices
- Manufacture clinical trial batches
- Set up contracts
- Keep the time -plan
- Deliver on budget
- Identify potential partners
- DELIVER THE PROMISES



# CONCLUSIONS

Being an entrepreneur implies:

- Hard work & good luck- if you don't believe in it, it won't happen
- Evaluate your risk and balance it
- Flexibility & uncertainty
- Enjoy your triumphs & don't let challenges bring you down
- Progress-time to market is essential
- Recognize your limits