

Continuous Oral Drug Delivery via OraFuse Device

Results from a Phase 2 Trial

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OraFuse Device

The first system for continuous, noninvasive oral drug delivery



**Custom-fit, reusable dental appliance
carrying a drug container**

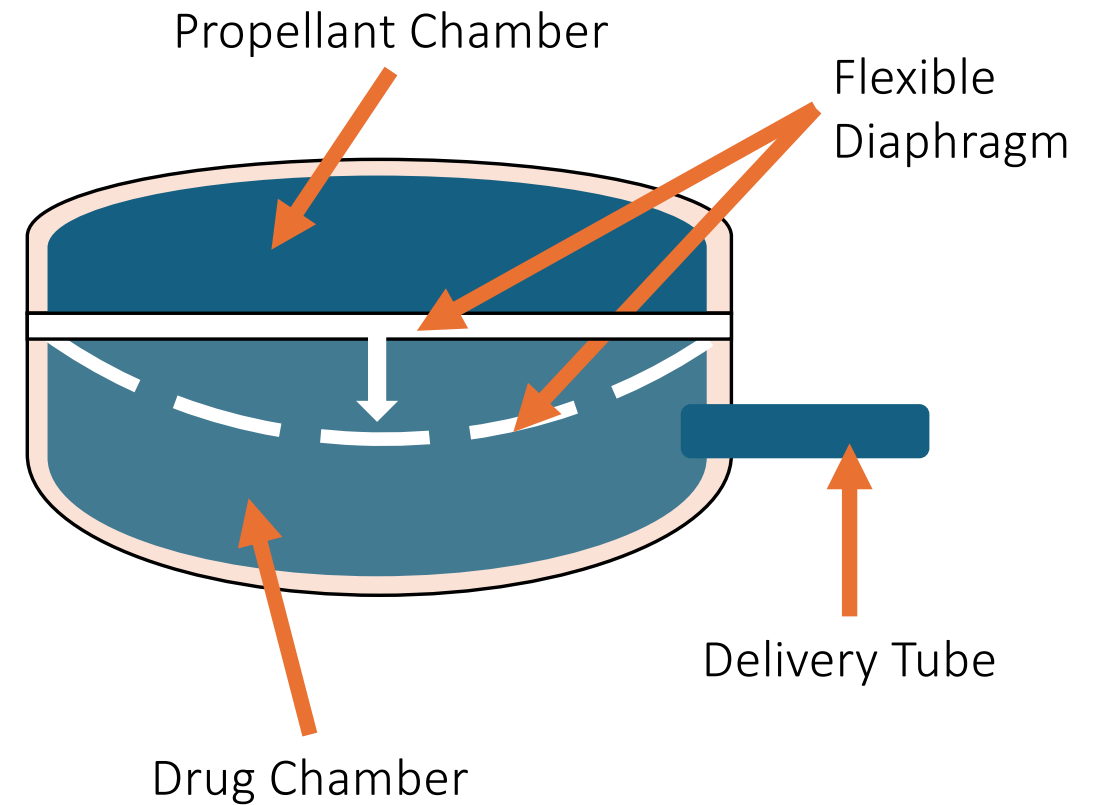
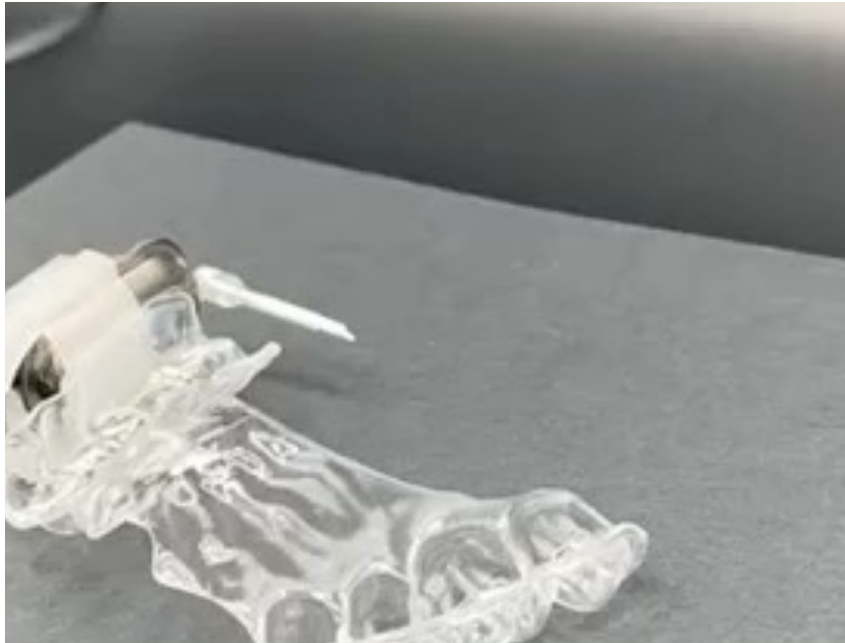
More Stable Drug Levels



**Single-use, pre-filled, disposable
micropump**

Safe and Non-invasive

OraFuse – Propellant-driven Micropump

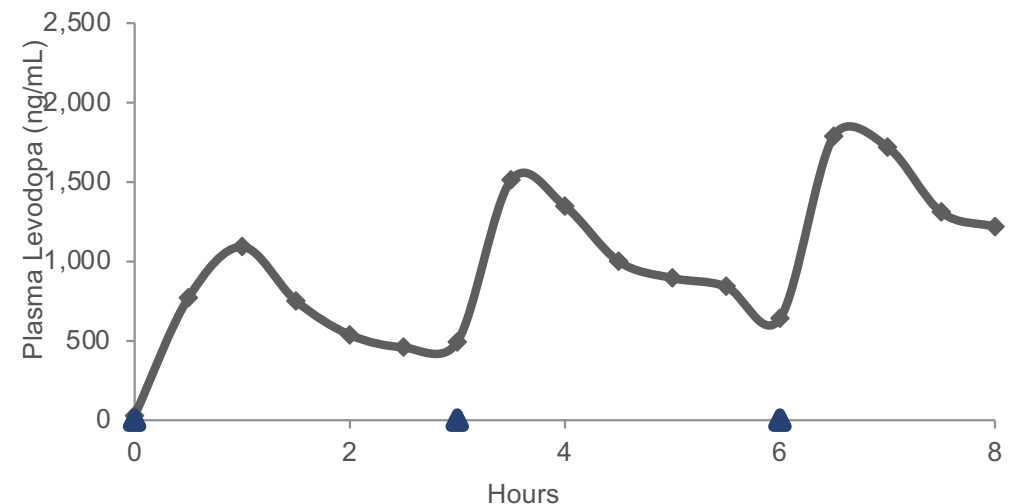


OraFuse Application for Parkinson's Disease

The Challenge

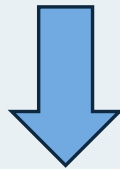
- The healthy brain has a near-constant level of dopamine. Intermittent oral LD therapy does not restore brain dopamine at a constant, physiologic level
- This is primarily due to the short half-life of LD and its absorption only in a short segment of the duodenum
- Advanced Parkinson's Disease patients can spend many hours per day in the 'off' state and/or with troublesome dyskinesia
 - Motor fluctuations include dose failure, early wearing off and sudden unpredictable switches
- Drug makers have failed to develop a controlled release oral form of levodopa that eliminates these symptoms
 - Controlled release pills provide only marginal benefit

Plasma Levodopa Levels with Intermittent Tablets



'Off' State (Underdosing)

Low plasma levodopa levels result in the return of motor symptoms
Tremor, rigidity, slowness



Goal is to increase time in the 'on' state

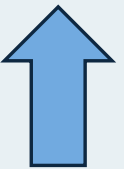
'On' State

Target plasma levodopa achieves desired results
Adequate control of motor symptoms



Dyskinesia (Overdosing)

High plasma levodopa levels result in dyskinesia, hallucinations, and nausea
Involuntary, erratic, writhing movements



Current Treatment Options for Advanced Parkinson's

Standard-of-care

Oral Therapeutics



Sinemet®
(carbidopa-levodopa)
Tablets



10 mg/100 mg

Off-patent: Pricing varies

Oral LD/CD Immediate Release ("IR") or Controlled Release ("CR") tablets

- ❌ OFF time
- ❌ Dyskinesia
- ❌ Disability
- ❌ Poor quality of life

Other Treatment Options

Duopa (Abbvie)



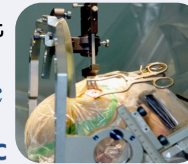
Continuous duodenal infusion of LD/CD via surgically implanted PEG tube using 100mL reservoir pump

- ❌ 97% Adverse Effects
- ❌ 17% post-op infection
- ❌ Surgically implanted
- ❌ Requires frozen storage

Deep Brain Stimulation (DBS)



Abbott
Boston
Scientific
Medtronic



Electrodes are inserted into a targeted area of the brain using MRI and brain cell activity recordings

- ❌ Highly invasive
- ❌ Expensive
- ❌ Risk of stroke/infection
- ❌ Frequent follow-up procedures

Subcutaneous Infusion (ABBV-951)



abbvie

Launching in EU in 2024
US NDA Application submitted in 2023.

Combination of foscarnidopa and foslevodopa administered subcutaneously with a syringe pump

- ❌ Infusion site reactions
- ❌ 22% dropout rate in clinical trial
- ❌ Increased hallucinations

Phase 2 Results: Safety, Tolerability and Usability

Patient Experience

94%

15/16 did not require assistance using OraFuse

88%

14/16 would continue to use OraFuse if given the opportunity

0

Deaths, dropouts, SAEs, clinically significant or persistent AEs

*"I would like to sincerely thank the entire team that develop this new system and the team that gave me the opportunity to participate in this study. **During the treatment with the new system I did not have any 'off' time. I was able to do all my activities without the fear of turning 'off'.** I was able to join again my class of water aerobics, that I needed to stop because I was getting stuck in the water, and I had to be rescued by the instructors.*

The usual 'off' that I have around lunch time disappeared completely, and this was very important for me because I usually work at that time. I really wish I was allowed to continue with this treatment now or at least to be able to start it again soon."

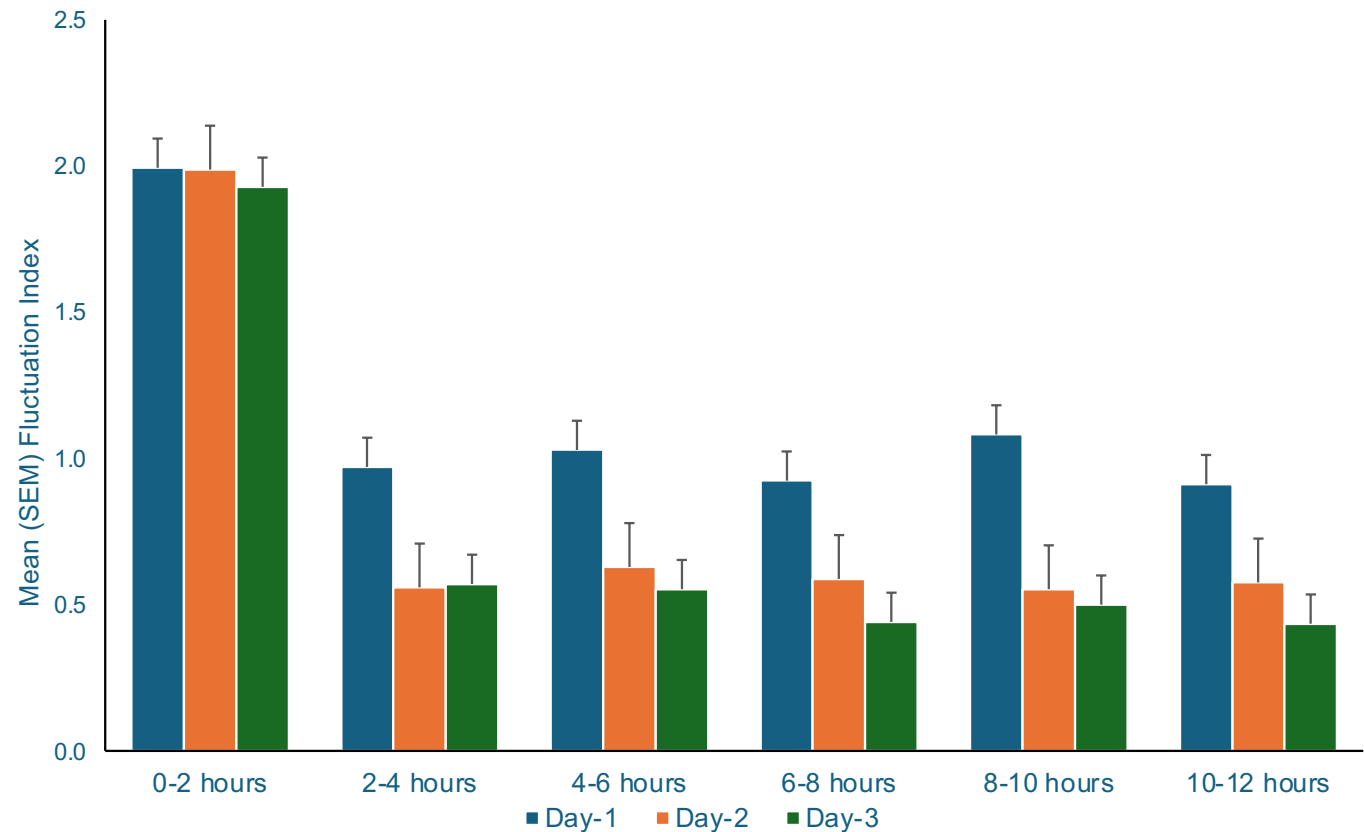
Source: Phase 2 Trial Patient Feedback

Phase 2 results: Primary Endpoint: Pharmacokinetics

Fluctuation Index by Time Interval

52%

*Average reduction
in Fluctuation Index
for all patients,
n=16
p<0.0001*

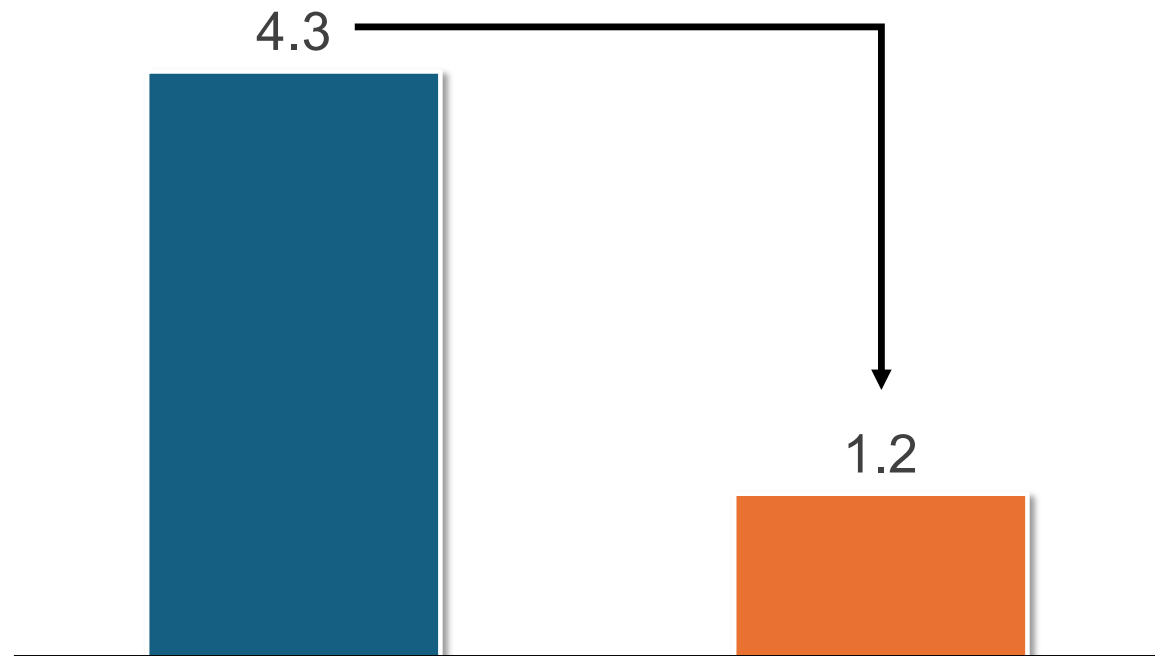


Phase 2 Results: Subgroup Analysis of the Most Advanced Patients

'Off' Time (Hours / Day)

72%

*Average reduction
in 'off' time for
patients with >2
hours of 'off' time at
baseline, n=11
 $p<0.001$*



Note:

The efficacy data must be interpreted cautiously as this is an open label, uncontrolled study in a small number of participants

OraFuse Delivers a High-Quality Patient Experience

OraFuse Benefits

- ✓ **Provides continuous dosing of LD/CD**
- ✓ **Non-invasive therapeutic delivery and symptom relief**
- ✓ **Patient friendly convenience:**
 - Pre-filled, disposable drug container on a retainer
 - Easily inserted and removed
- ✓ **3 products with 3 delivery rates:**
 - Allows for individual dosing

Patient Feedback¹

*"The system is easy to use. **I can feel the continuous doses especially during a physical effort.** I can walk for more distance with an upright posture. There is a clear improvement of my voice."*

*"**During the two days of OraFuse use, all the phases were 'on'.** For the first time on the third day I saw my right arm swinging with the right rhythm; something I haven't seen in 2 years."*

*"[I liked] not having to be aware of the medication. **It gives freedom by not having ups and downs.** I can go out alone without fear."*

*"For me this was like a new life, the realization that **I am 'on' almost the whole day** was just great and life-affirming."*

Source: Company materials

Note: Patient feedback received after the completion of the Company's phase 2 trial

OraFuse Next Steps – Industry Partnerships

Parkinson's Disease – Industry Partnership

- Seeking industry partner to lead Market Access efforts
- Seeking financial support for Phase 3 Clinical Trial
- Seeking Contract Manufacturers for OraFuse device (pending industry partnership)

Xerostomia – Research & Development and seeking Industry Partnership

- Patients with Head and Neck Cancer who have had Salivary Glands destroyed from radiation
- Patients have severe dry mouth, causing difficulties eating, sleeping and increased risk of choking
- OraFuse delivers saliva-stimulating enzymatic gel throughout the day and night
- Fully 3D-printed device, significantly reducing manufacturing costs
- Simplified regulatory pathway
- Seeking Dental, Oral Medicine and Oncology partnerships to develop Market Access
- Seeking Contract Manufacturers for reformulation and manufacturing of Oral Gel



Innovation

*The key to sustainable
healthcare*