PharmaShell® –
Enabling once-monthly and once-quarterly semaglutide depots

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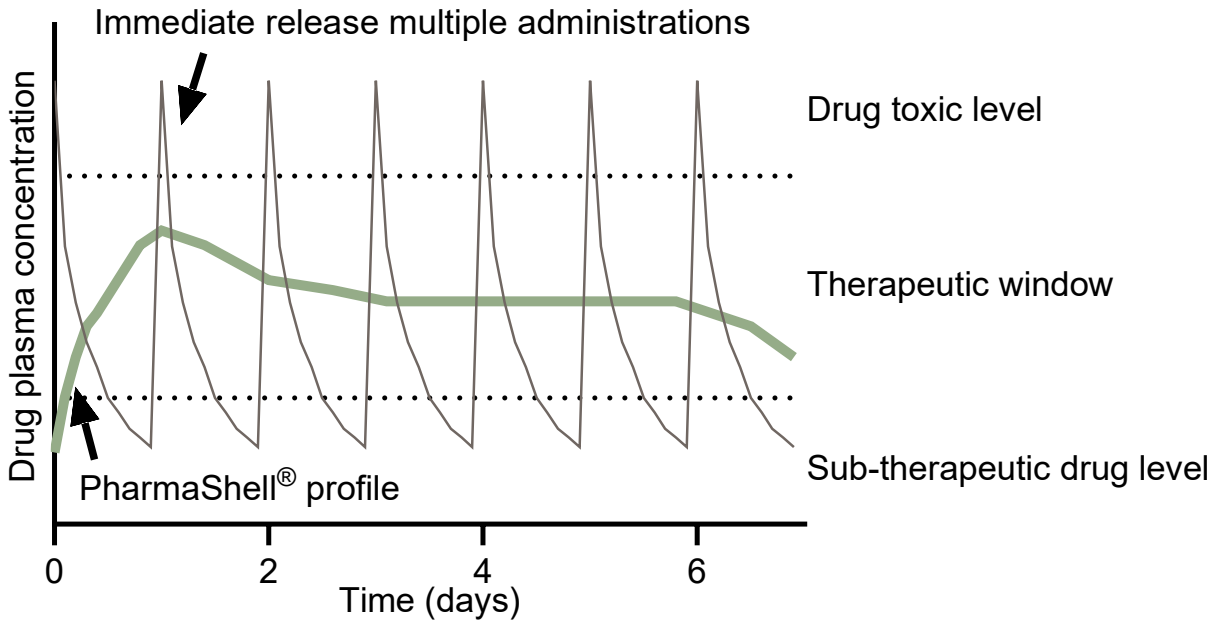
In this talk

- PharmaShell® platform and release mechanism
- Clinical proof-of-concept (liraglutide)
- Programmable profiles: once-monthly and once-quarterly semaglutide (modelled to humans)

More than **50% of patients** do not follow their treatment correctly

10.1001/jama.2018.19271

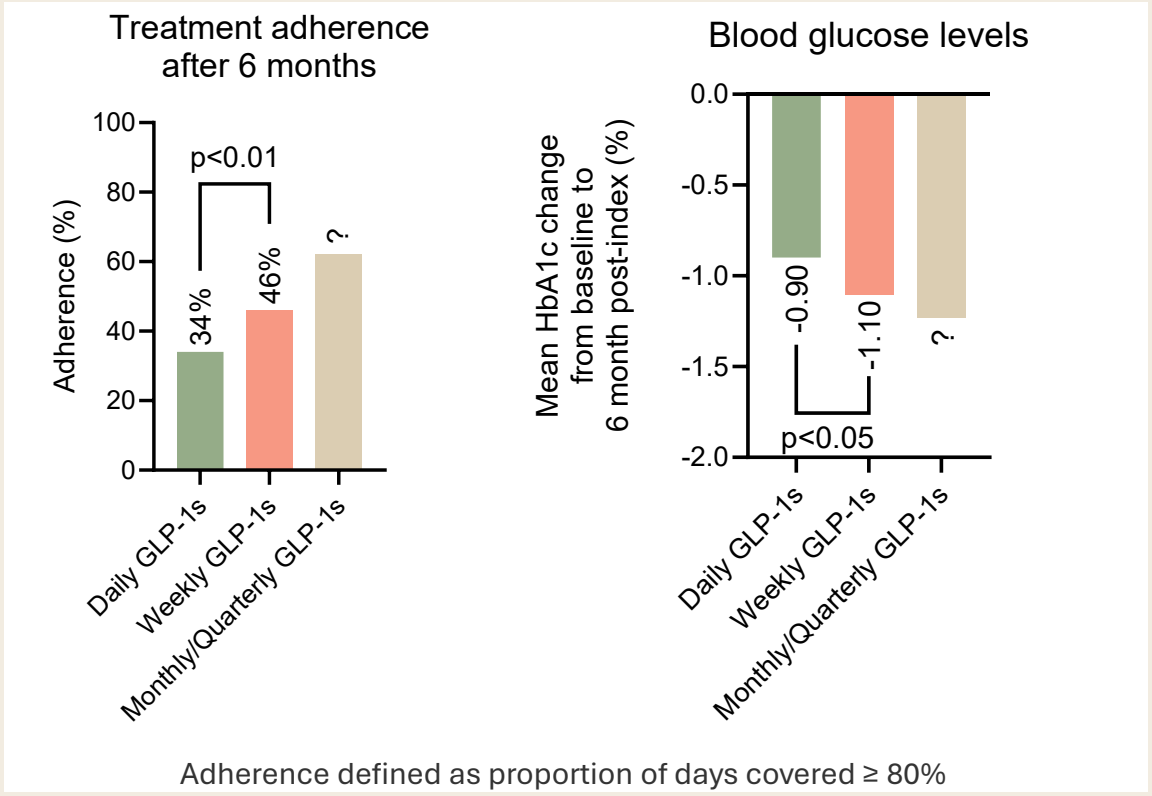
Smarter Care with Long-Acting Injectables



GLP-1 as an example

Why longer-acting injectables matter

- GLP-1 case study: weekly GLP-1 treatments significantly increased adherence compared to daily treatments
- Once a month or quarterly dosing can further boost adherence, offering potential for better patient outcome
- Long-acting depots of peptide therapeutics are challenging
  - Narrow therapeutic window
  - Ease of use
  - Peptide stability



Polonsky et al. Diabetes Ther 13, 175–187 (2022) daily and weekly figures adapted from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8776963/figure/Fig3/
http://creativecommons.org/licenses/by-nc/4.0/

PharmaShell® at a glance

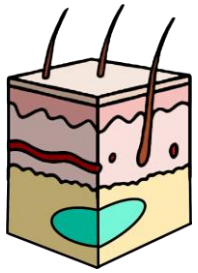
- PharmaShell® platform programmable profiles: once-monthly to once-quarterly
- Clinical PoC: once-monthly liraglutide demonstrated in Phase 1
- Suitable for wide range of molecules
- Broad internal and partnered programs, incl. Moderna mRNA program
- GMP-certified site and QC facility
- Platform protected by a comprehensive patent portfolio

PharmaShell® technology

FORMULATION

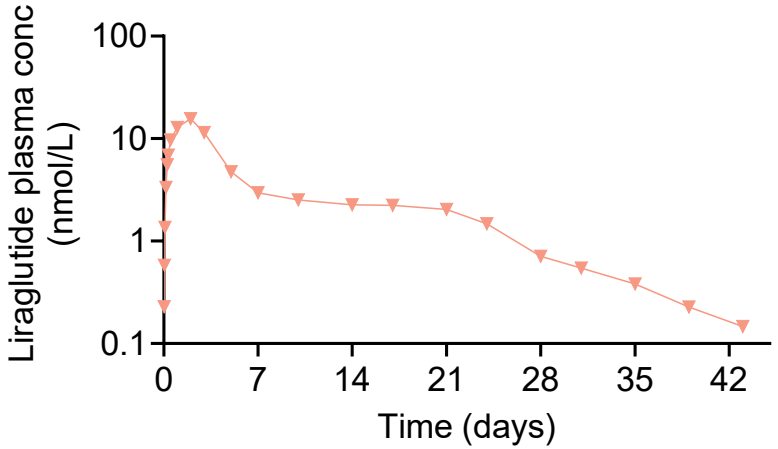
Tailored formulations:

- Micronized active pharmaceutical ingredients (APIs)
- Nano-thin coatings
- Biodegradable



SUBCUTANEOUS OR LOCAL INJECTION

The coated API particles create a depot at the injection site

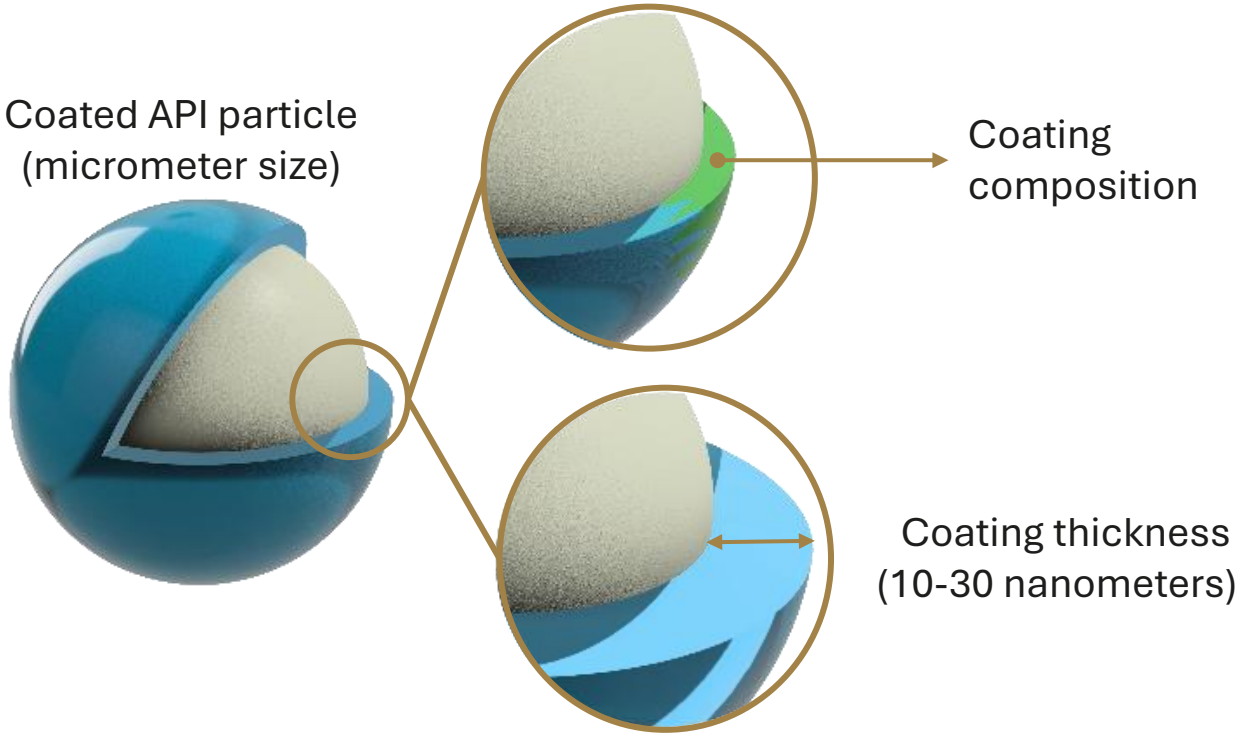


LONG-ACTING

The active pharmaceutical ingredient (API) gradually becomes available for release over time as the coating is slowly dissolved

PharmaShell® technology

- Designed for high-load peptide depots
- Nano-thin coating around every individual API particle
- The properties of the coating controls the duration of the depot
- The coating protects the API



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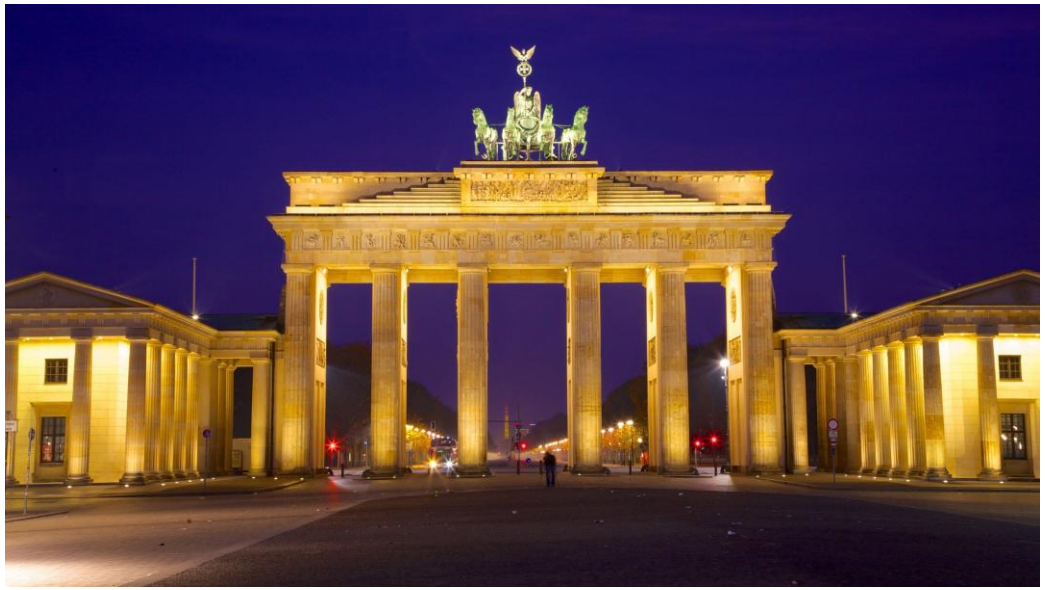
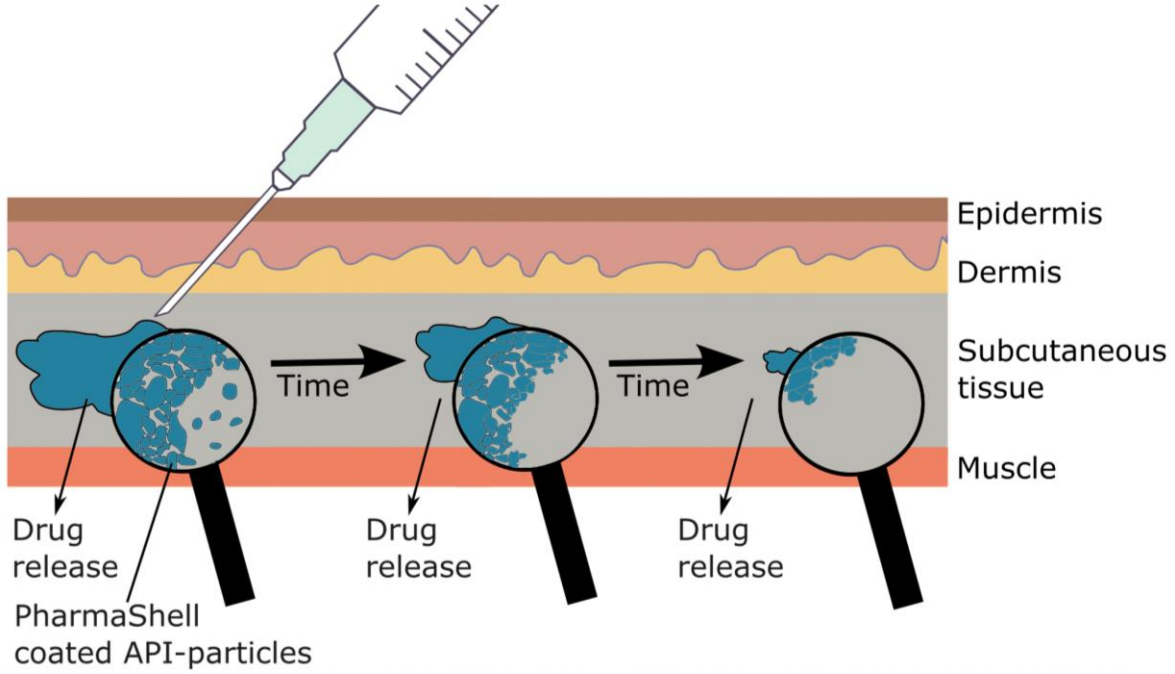


*If the Brandenburg Gate (26 m tall) were a PharmaShell® particle at the same scale, the coating would correspond to an additional layer of only about **3 cm**.*

Administration

- PharmaShell® is administered as a suspension
- The depot remains at the injection site
- PharmaShell® coating gradually dissolves, releasing the API for systemic circulation
- The coating dissolves into ions which are eliminated via urine, faeces and sweat

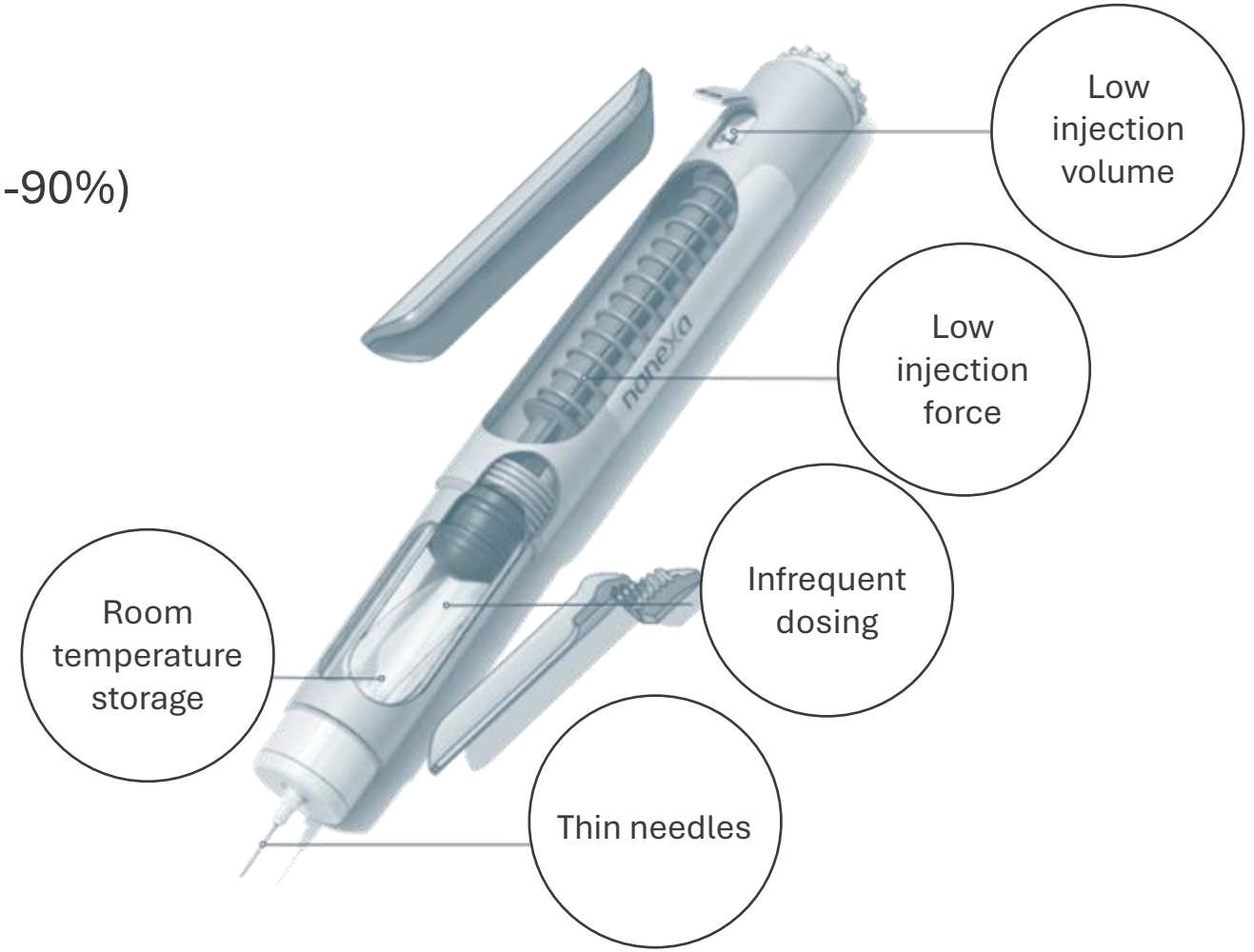


PharmaShell®

Patient-friendly dosing

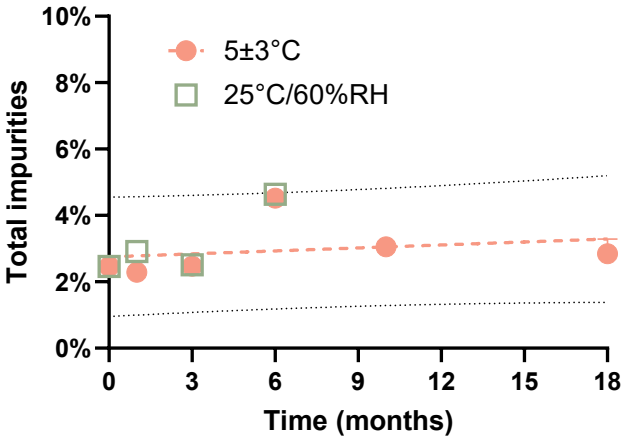
- <1-mL injections due to high API load (70-90%)
- Thin needles, 30G
- Room temperature storage

Phase 1: powder and a solvent for injection

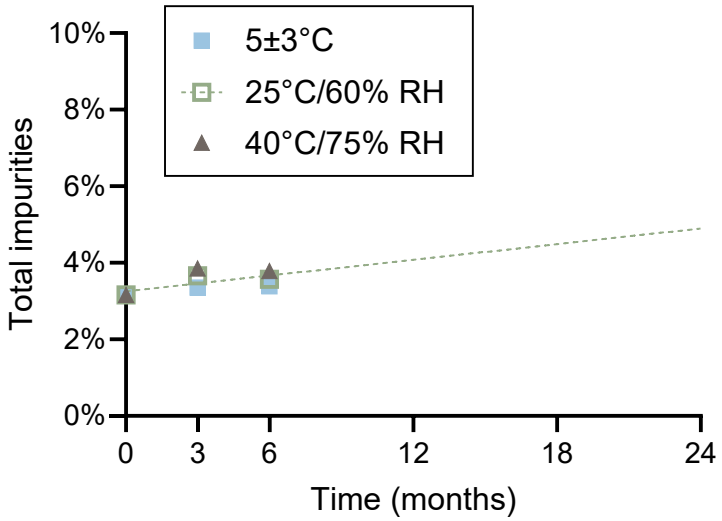


Target commercial product

Stability



Real-time data for 6 months at 25°C/60% RH, PharmaShell® coated liraglutide in clinical trial material



Accelerated data for 6 months at 40°C/75% RH, PharmaShell® coated liraglutide development material

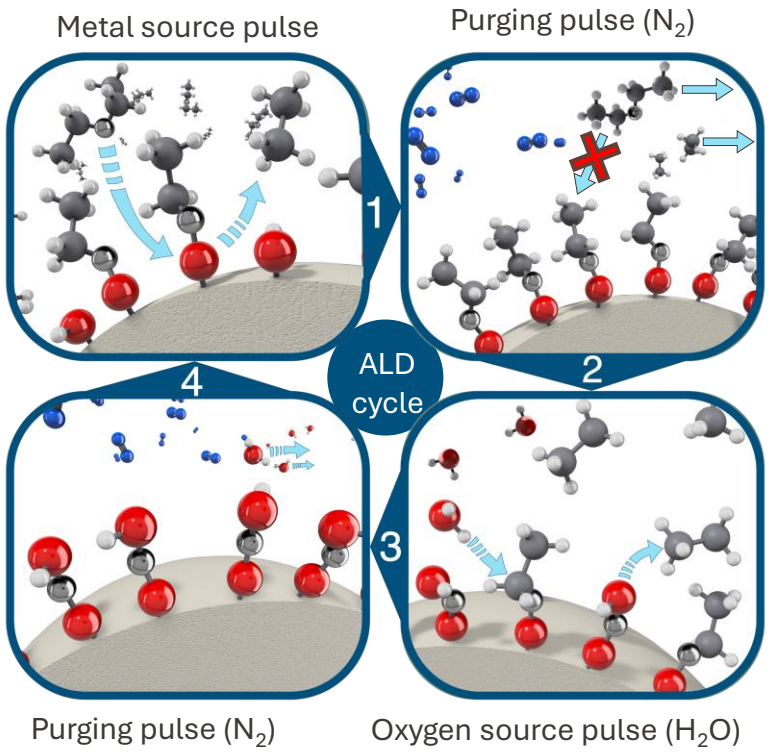
The PharmaShell® coating preserves product quality, omitting the need for cold storage requirements

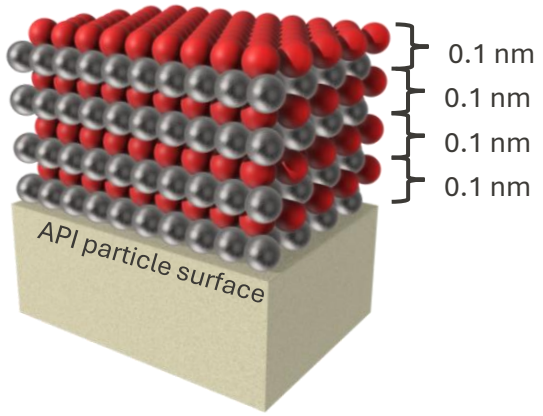
The Chemistry behind PharmaShell®

Atomic Layer Deposition

ALD is made up of pulses each with its own function:

- Two types of pulses
  - Precursor - growth occur
  - Purging – by product and excess removed
- A set of, typically 4, pulses makes up an ALD cycle

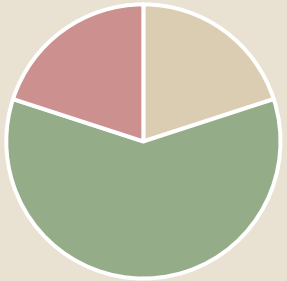




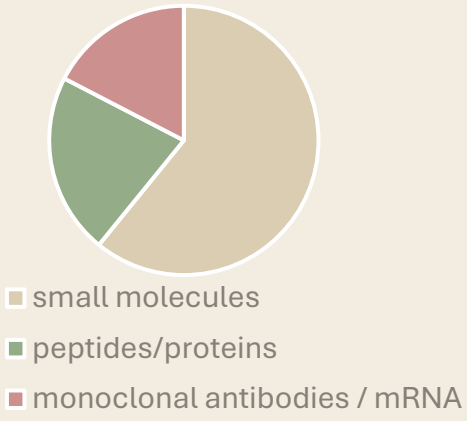
PharmaShell® development

- PharmaShell® has been shown to be suitable for peptides and a wide range of APIs, including small molecules, proteins, oligonucleotides, and mAbs
- 3 clinical Phase 1 studies: NEX-18, NEX-20, NEX-22

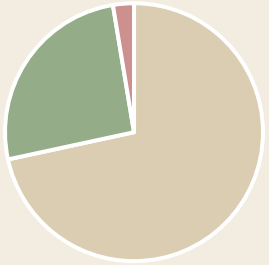
Partner project pipeline



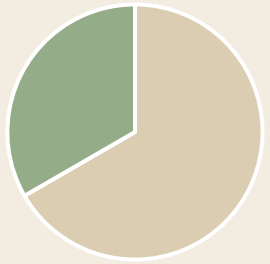
>30 coated APIs



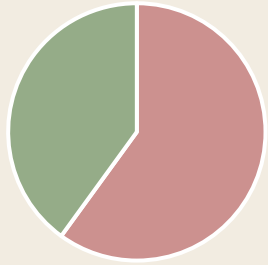
>400 ALD batches



3 clinical studies



>55* preclinical studies



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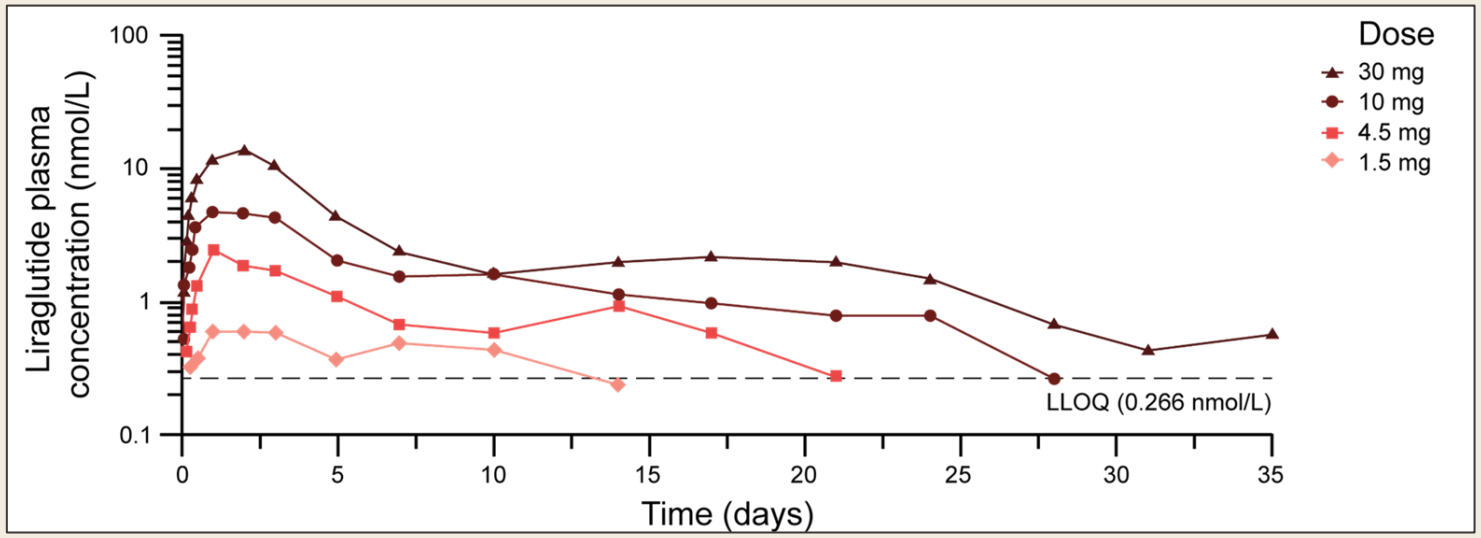
*updated 22MAY2026

From platform to proof-of-concept

Liraglutide with PharmaShell® shows clinical exposure over 36 days

85th American Diabetes Association , Chicago June 22nd, Poster 1975-LB



- Phase 1 results in GLP-1 naïve participants with type 2 diabetes, n=3
- Release of liraglutide over 36 days after a single subcutaneous injection
- Dose linearity in exposure and C_{max}

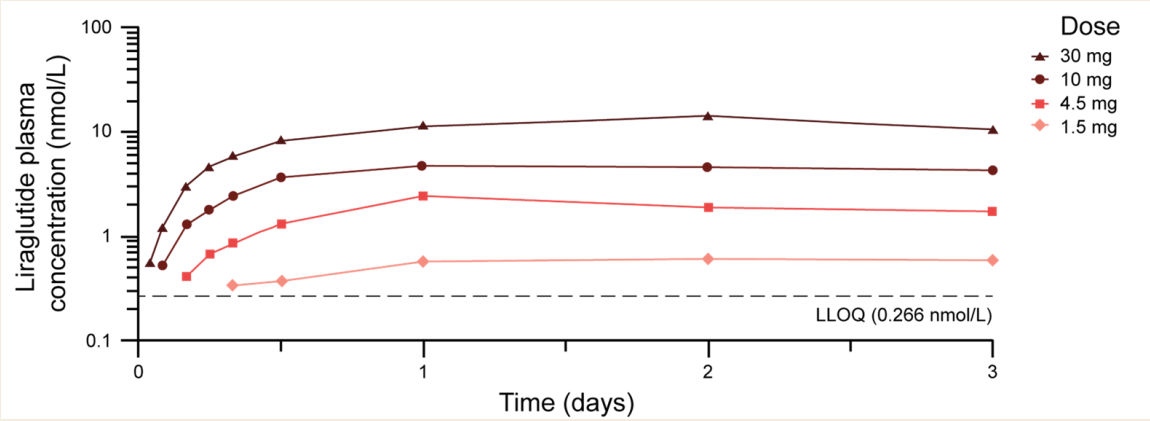
Positive Proof of Concept for a once monthly injectable GLP-1

From platform to proof-of-concept

Liraglutide with PharmaShell® was well tolerated

- Subcutaneous NEX-22 was generally well tolerated
- No nausea or diarrhea reported
- Decreased appetite and occasional heartburn reported as GI adverse effects
- Injection-site reactions, most commonly erythema, generally resolved within ~1 week; investigator-assessed as not clinically significant

Can a delayed T_{max} limit the GI adverse effects?



Positive Proof of Concept for a once monthly injectable GLP-1

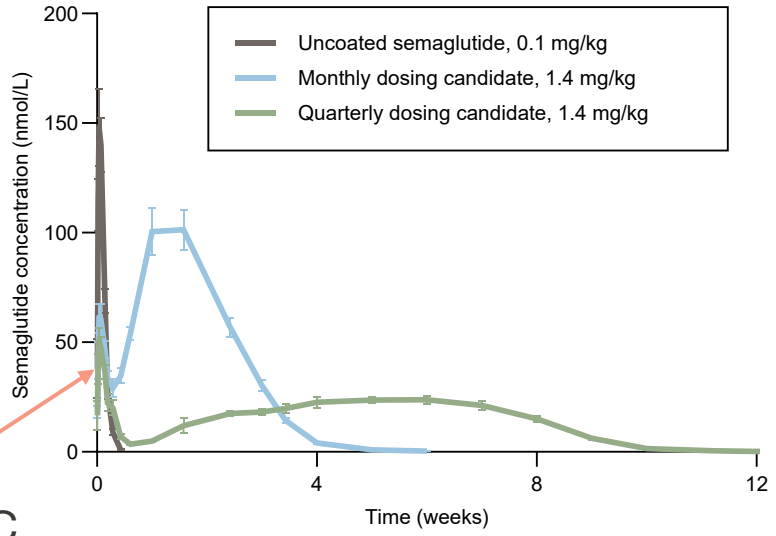
Taking the concept beyond liraglutide

- A strategic shift from PharmaShell® liraglutide to PharmaShell® semaglutide was done in 2025 due to following reasons:
  - Market and partner alignment.
  - Superior clinical efficacy, not only in type 2 diabetes but also in obesity.
- Clinical proof-of-concept for PharmaShell® liraglutide is expected to be valid also for other peptides such as semaglutide.
  - Similar dose ranges.
  - Peptide backbone are very similar.
- Weekly marketed semaglutide has a narrow peak-to-trough ratio ($C_{max,ss}/C_{min,ss}$) of 1.8.
  - A long-acting injectable needs to be within this ratio to achieve same efficacy.

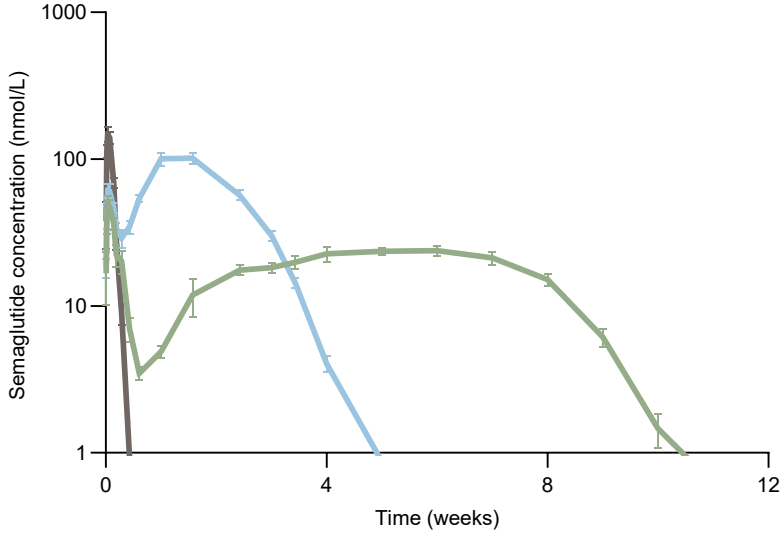
PharmaShell® coated semaglutide in rats

- **Study Formulations:** PharmaShell® coated semaglutide formulations aiming for monthly and quarterly dosing
- **Test Animals:** Male Sprague Dawley Rats, n=4 per formulation
- **Administration:** Single dose, 1.4 mg/kg, subcutaneous
- **Sampling:** Blood sampling at 0 to 3 months
- **Analysis:** Analysis of semaglutide plasma concentrations after 1.5 and 3 months

Linear scale



Logarithmic scale



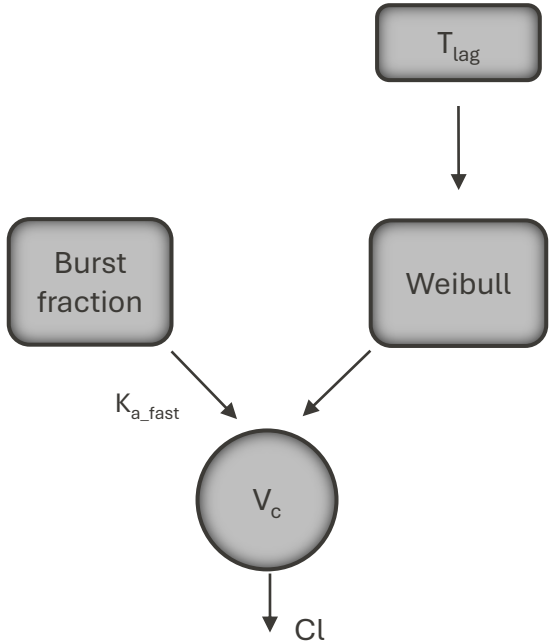
Low initial burst/C_{max}

From rat PK data to human simulation

Modelling and simulation of human plasma profiles

- Human steady state simulation was based on published data[1] (see Table below).
- Parameter related to absorption was translated from preclinical data using a double Weibull function and a 2-compartment model based on literature data.[2]
- The dose was adjusted to give a plasma C_{avg} 79.2 nmol/L.

Parameter	Value	Reference
Central volume	3.59 L	From Overgaard et al
Peripheral volume	4.10 L	From Overgaard et al
Clearance	0.0348 L/h	From Overgaard et al
Inter compartmental clearance	0.304 L/h	From Overgaard et al
Weight	81.9 kg	From Overgaard et al

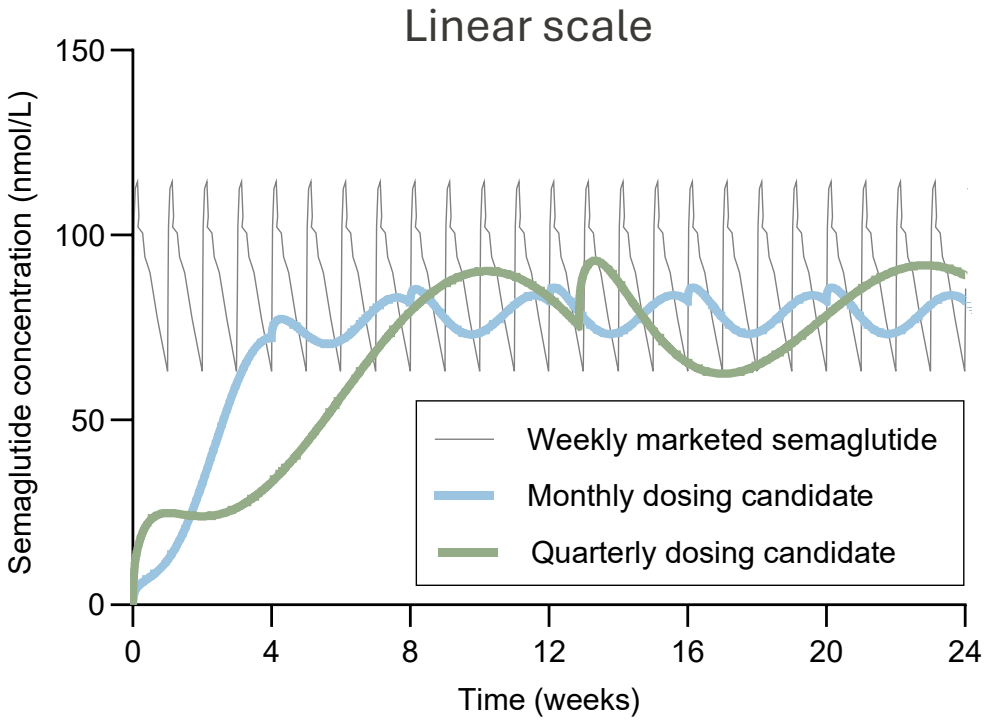


[1]Overgaard et al (DOI: 10.1007/s13300-019-0581-y)
[2]Kim et al (DOI: https://doi.org/10.1007/s40005-024-00717-3)

Simulation of repeated dosing in humans

Monthly or quarterly dosing

PharmaShell® semaglutide outperforms marketed semaglutide's narrow peak-to-trough ratio when dosed monthly (every 28 days) or quarterly (every 90 days).



Formulation	Dose (mg)	Peak-to-trough ratio
Weekly (Q1W) marketed semaglutide[1]	2.4	1.8
Q1M PharmaShell® coated semaglutide	12.3	1.2
Q3M PharmaShell® coated semaglutide	43.7	1.5

1) https://www.ema.europa.eu/en/documents/assessment-report/wegovy-epar-public-assessment-report_en.pdf Table 9 and 10

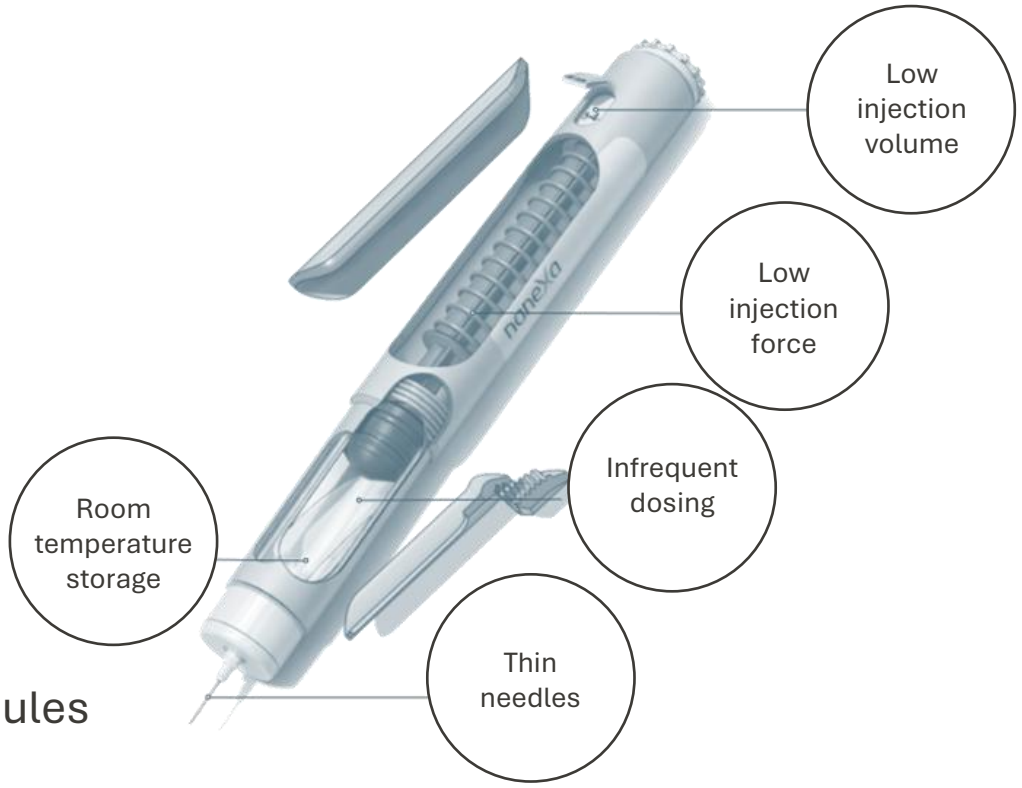
PharmaShell® semaglutide

- Simulated repeated-dose peak-to-trough ratios were 1.2 and 1.5 for monthly and quarterly dosing, respectively, as compared to 1.8 observed for weekly dosed marketed semaglutide.
- The excellent narrow peak-to-trough ratios suggest that monthly and quarterly dosing of PharmaShell® semaglutide is superior to weekly dosed marketed semaglutide.
- Next step is to advance these formulations into Phase I clinical evaluation with safety and PK as primary end-points.

Beyond GLP-1: long-acting formulations for your program

PharmaShell® enables safe and convenient long-acting peptide depots

- **Tailored depots**
  - Monthly or quarterly dosing
  - Applicable for narrow therapeutic window drugs
- **Patient friendly**
  - Thin needles, 30G
  - <1-mL injections due to high drug loads
  - Room temperature storage
- **Manufacturability**
  - Suitable for wide range of APIs including sensitive molecules
  - Protects the API during storage and in the depot
  - In-house GMP manufacturing and QC facility



Target commercial product

Thank you for listening!

Do you want to know more or initiate partner discussions?

Reach out to:
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