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PharmaShell®

The high drug load delivery system enabling the next generation long-acting injectables through atomic layer precision

nanexa

Nanexa in brief

Founded in Uppsala, Sweden in 2007, Nanexa is a drug development company for Long Acting Injectables based on the unique proprietary PharmaShell® drug delivery system

Chairman of BoD: Dr. Göran Ando (former Chairman of the BoD Novo Nordisk and EVP Pharmacia&Upjohn)

Management team with extensive experience from the global pharma industry

Strategic partnership with Applied Materials Inc. to facilitate seamless up-scaling of the PharmaShell ALD process to commercial manufacturing scale

Nanexa's solution

Nanexa's drug delivery system, **PharmaShell®**, encapsulates drug particles with an extremely thin coating with defined and low solubility, controlling the release of the drug substance

Two-streamed business model based on developing products in-house as well as licensing to external parties

PharmaShell®

Product licensing

Internal development of LAI products (improved versions of existing drugs)

Technology licensing

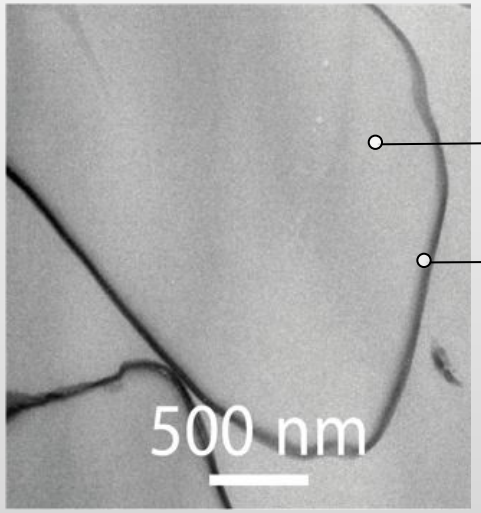
License to partner companies

LCM or NCE

Nanexa highlights

- PharmaShell® patents secured on major markets, with several more pending approval
- Nanexa has started its first clinical study with a phase I first-in-human (FIH) study during Q2'21
- GMP-certified facility ensuring supply throughout clinical development
- Listed on Nasdaq First North in Stockholm

PharmaShell® – The high drug load delivery system enabling the next generation long-acting injectables through atomic layer precision



TEM image of PharmaShell coated API particle

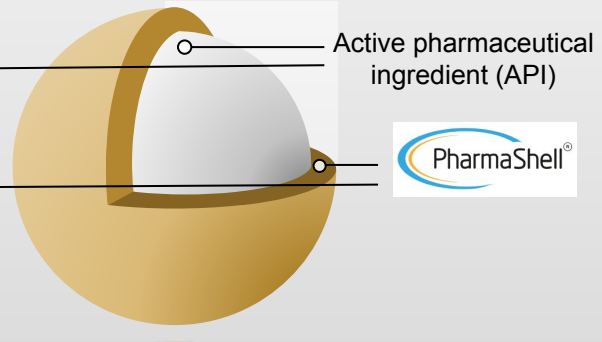
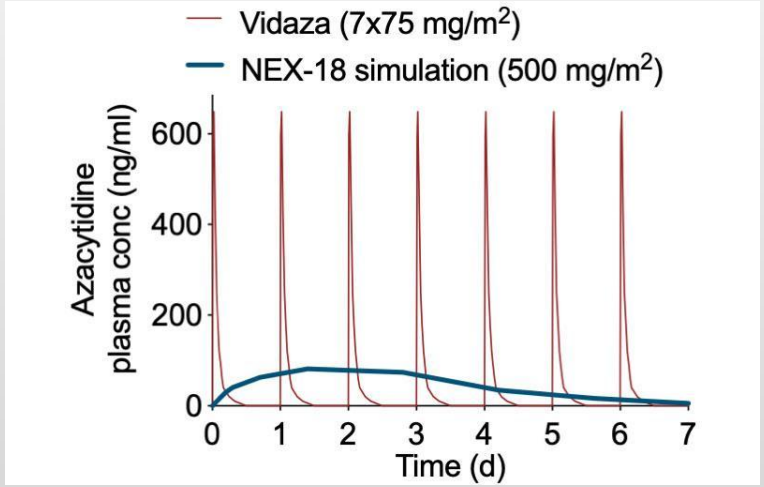


Illustration of PharmaShell's nanometer thick coatings

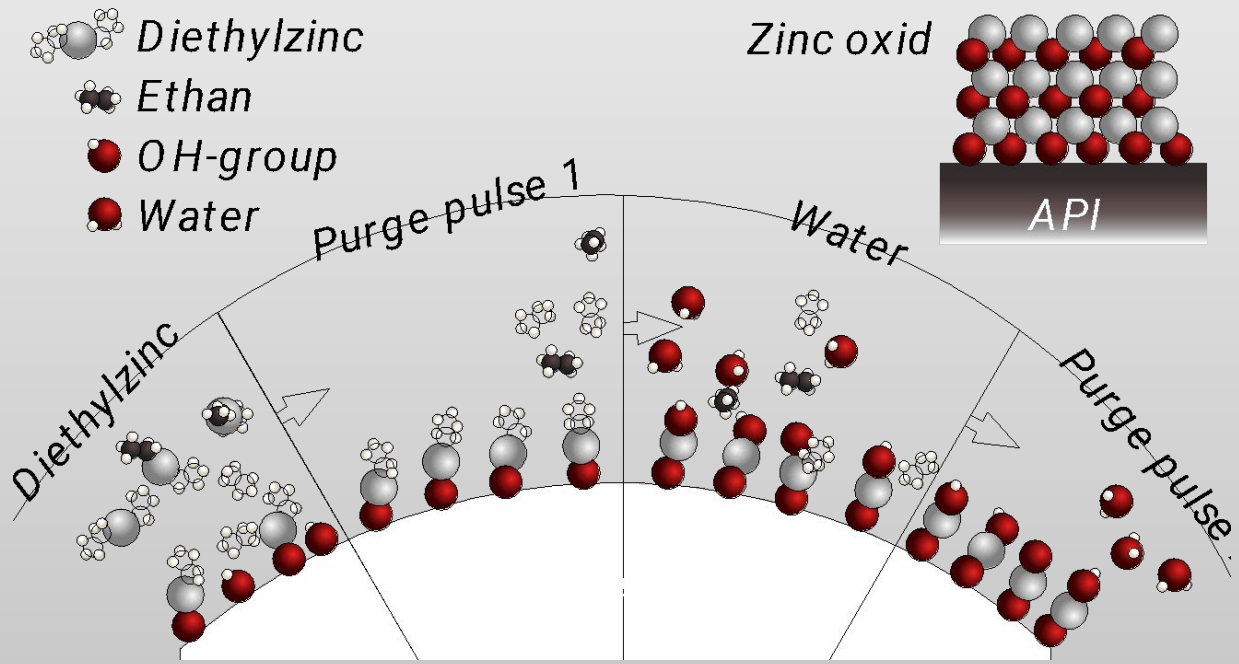


Concept data illustrating the avoidance of high and low plasma concentrations by using PharmaShell

- Drug delivery system encasing active substance microparticles with thin coatings (10—50 nm) of slow-dissolving inorganic oxides
- System based on Atomic Layer Deposition (ALD) technology, enabling Nanexa to control the thickness of the drug's shell with high precision and determine the rate of release of the drug in advance

- Immediate release formulations are converted into long-acting injectables with enhanced properties
- Drug concentrations are kept within the therapeutic window to achieve the maximum benefit

Atomic Layer Deposition (ALD) is a gas phase technique for making well defined coatings of inorganic oxides



Process features

- Gas phase process
- Low temperatures
- Dry process
- No need for solvents
- No need for purification steps
- Scalable

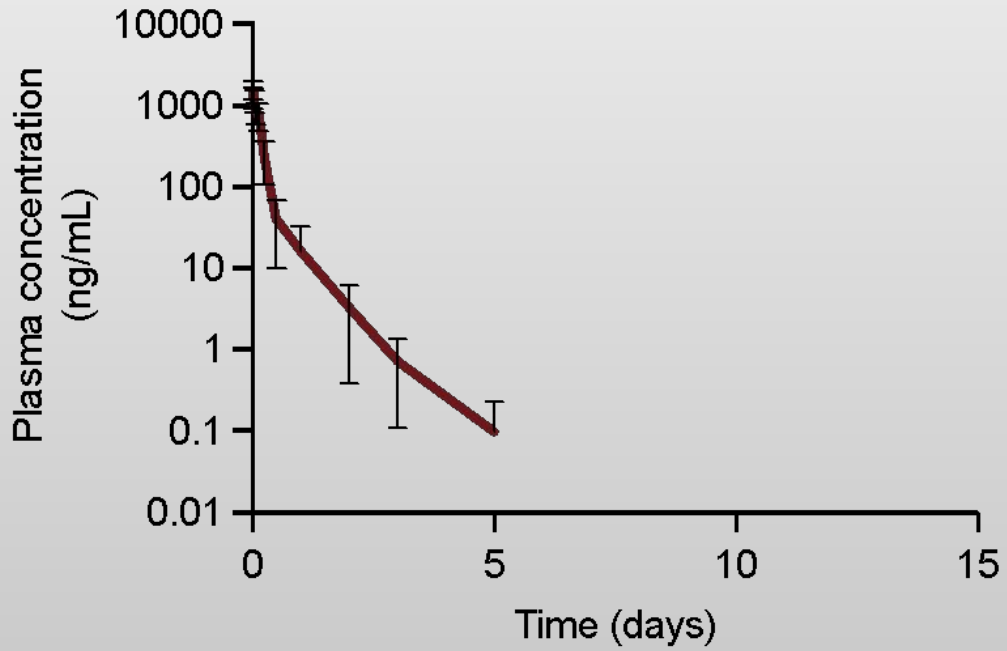
PharmaShell®: customized control enabling key benefits

- **Versatility** – applicable on a wide range of API characteristics
  - Small molecules
  - Biologics – peptides and proteins, etc
- **Customised** depot length
  - weeks, months or even longer
- **Controlled** drug release, minimises side effects and enables:
  - Minimize and control initial drug release
- **Protects** drug substance in-situ
  - Dense coating prevents hydrolysis or enzymatic cleavage
- **High** drug loads (up to 90%), enabling:
  - Minimised injection volumes
- **Flexibility** in respect of administration site
  - Subcutaneous or intramuscular administration for systemic exposure
  - Local administration, e.g. intratumorally, for local effect

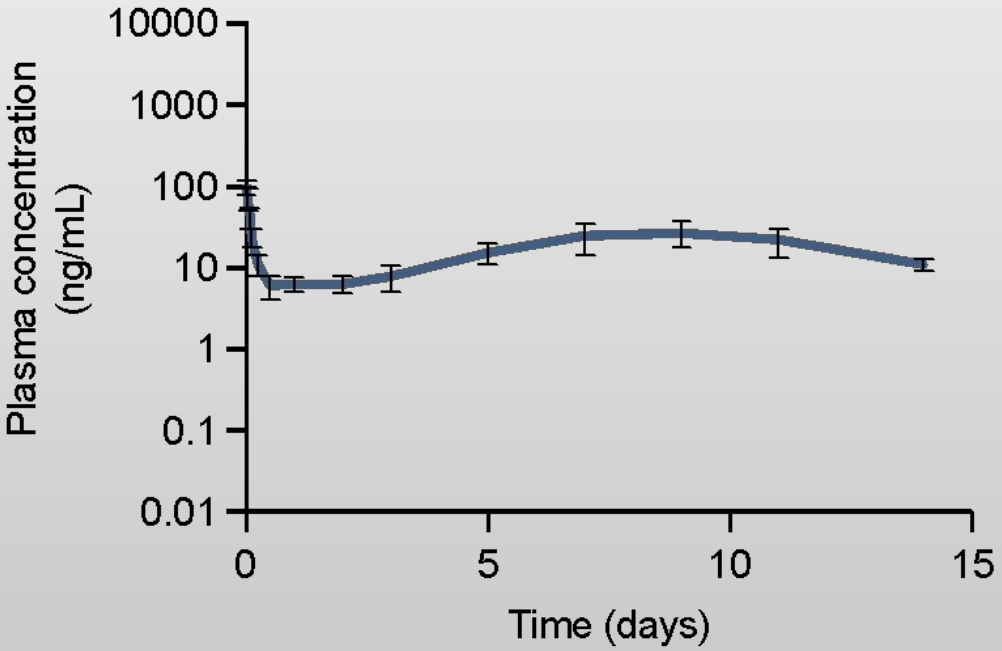
Subcutaneous lenalidomide, 10 mg/kg single injection, rats, n=6

NEX-20: Lenalidomide pharmacokinetics

Non coated lenalidomide



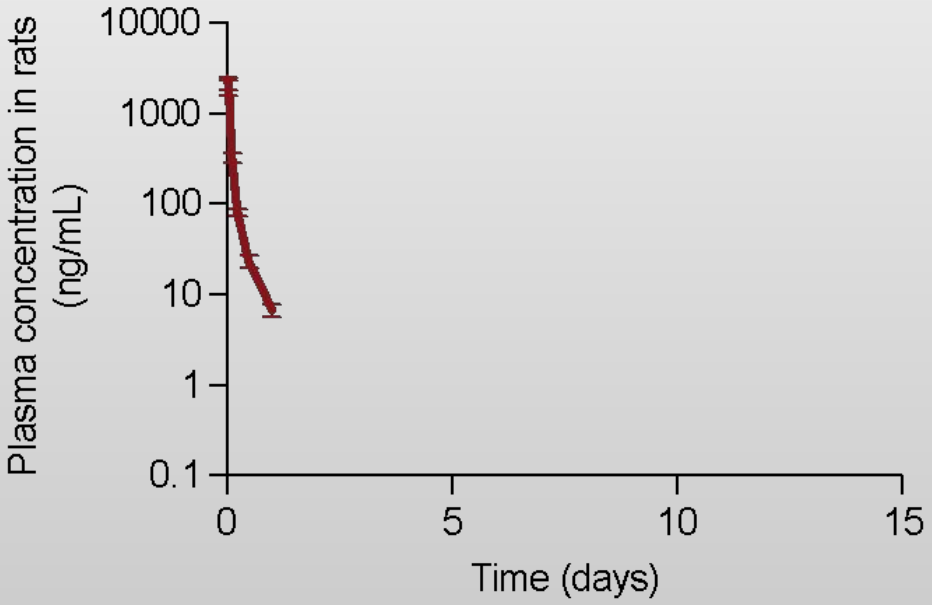
PharmaShell® controlled release coated lenalidomide



Subcutaneous NEX-20, controlled release coated lenalidomide, 10 mg/kg single injection, rats, n=6

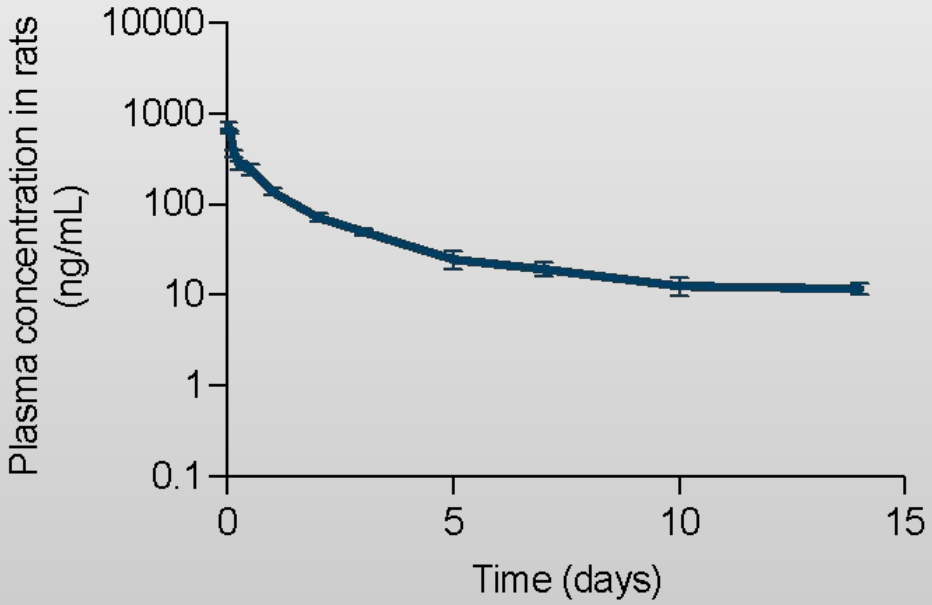
NEX-18: Azacitidine pharmacokinetics

Non coated azacitidine



Subcutaneous azacitidine, 5.0 mg/kg single injection, rats, n=6

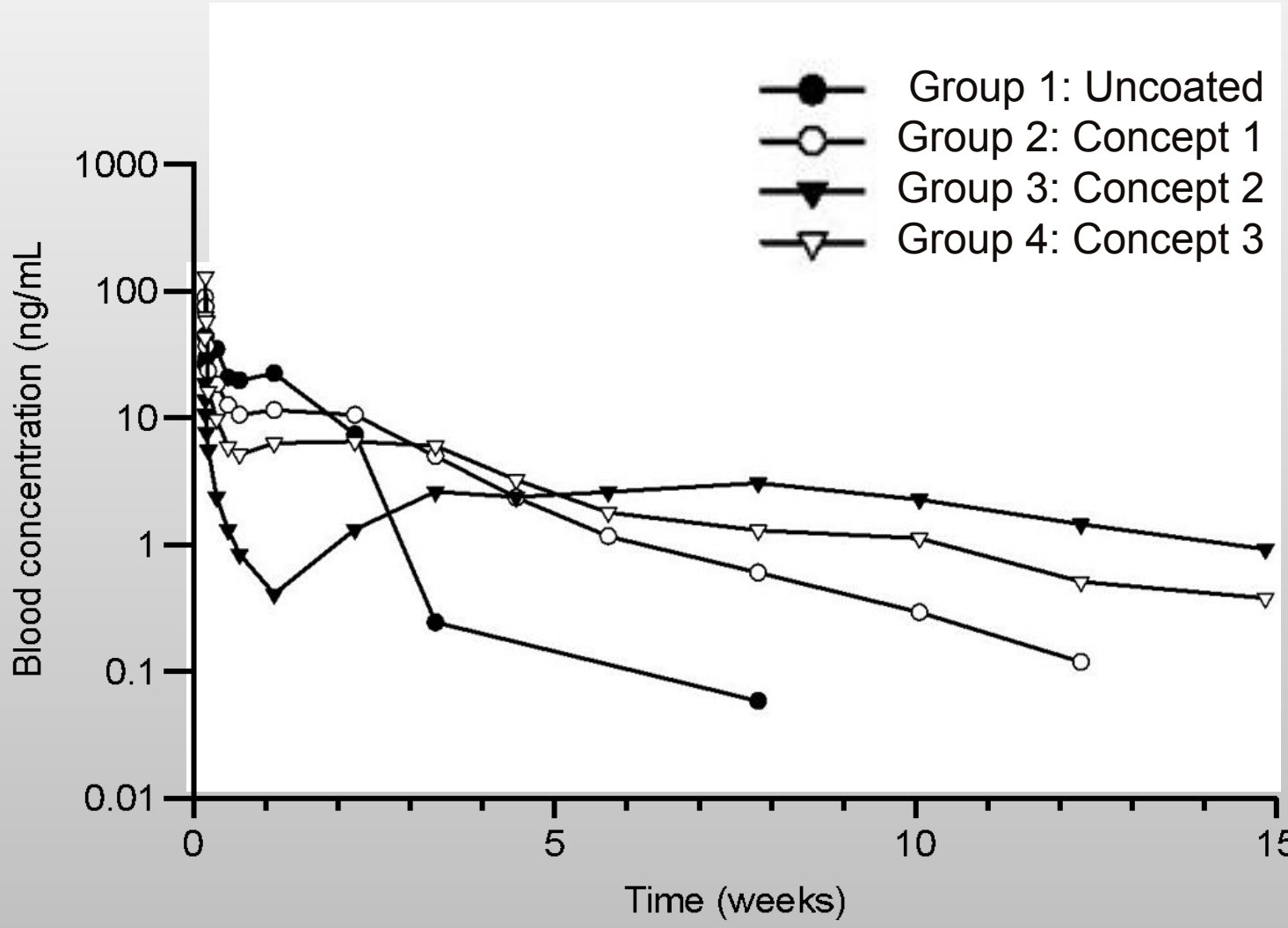
PharmaShell® controlled release coated azacitidine



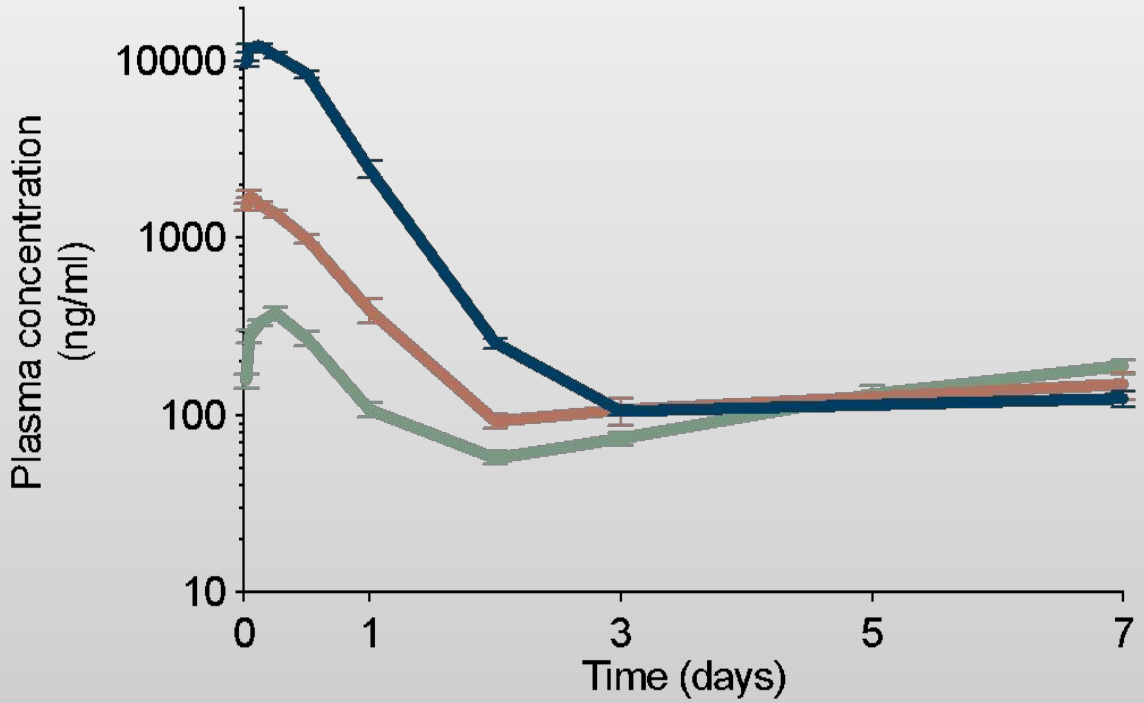
Subcutaneous NEX-18, azacitidine sustained release formulation, 13.5 mg/kg, single injection, rats, n=6

Source: Nanexa on file

PharmaShell® - Several months duration of coated APIs



PharmaShell® - Control of initial drug release

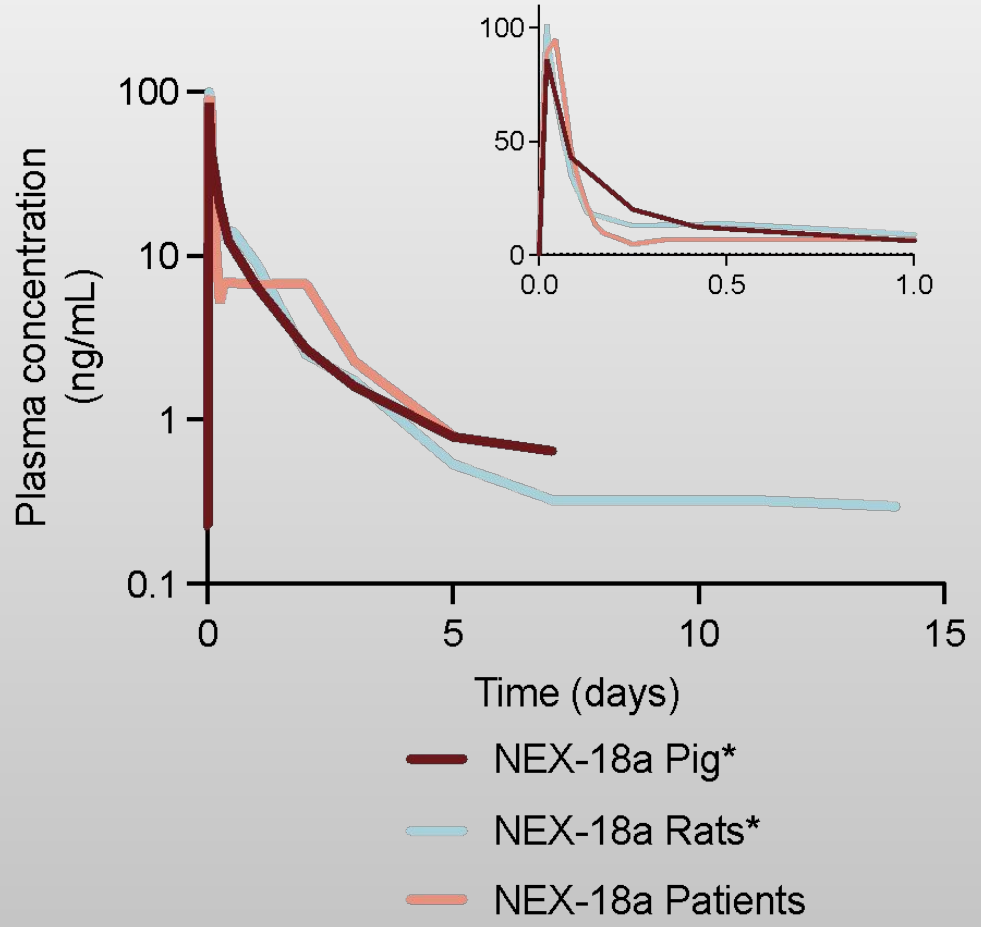


Legend	Dose	Drug load	Nanoshell thickness	Release first 48 h (% of total dose)
	10 mg/kg	82%	10 nm	47%
	10 mg/kg	81%	10 nm	6%
	10 mg/kg	84%	10 nm	2%

Pharmacokinetic proof of concept: rats-minipigs-humans

Controlled release of PharmaShell® coated azacitidine

Comparable release profiles post subcutaneous administration in rats, pigs and humans

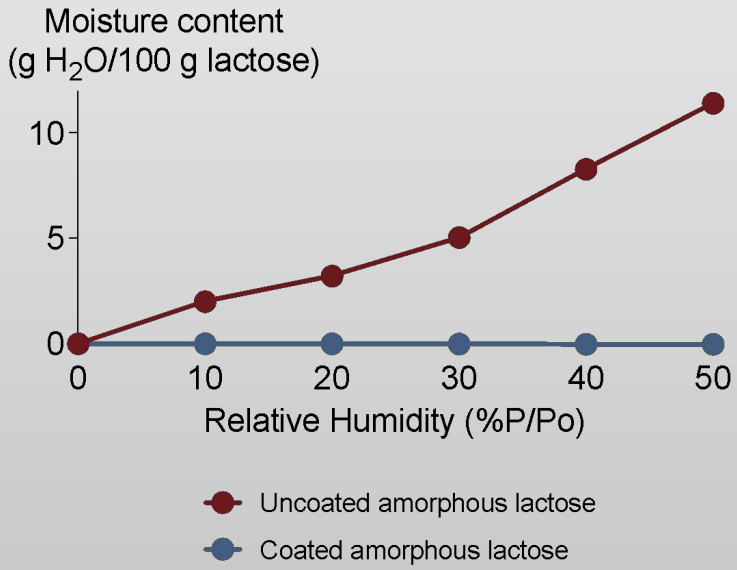


*Plasma concentrations has been adjusted using the least square method to correct for species and dose differences.

PharmaShell® coating acts as moisture barrier. – prevents in situ hydrolysis

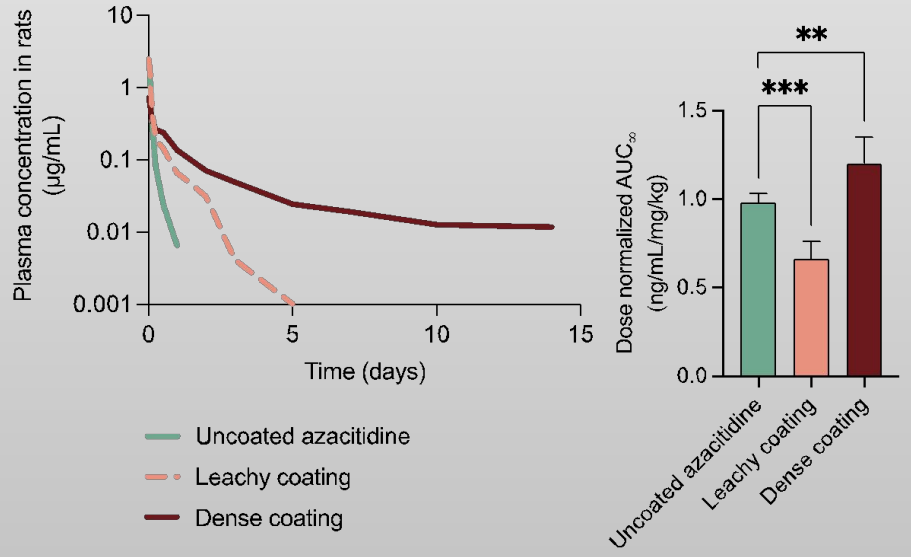
Coated amorphous lactose

- Amorphous lactose is highly hygroscopic
- ALD-coating prevents sorption studied with dynamic vapor sorption (DVS)



Controlled release coated azacitidine

- Azacitidine is rapidly hydrolyzed in contact with water
- Increased AUC for dense coating compared with uncoated azacitidine – coating protects from hydrolysis
- Decreased AUC for leachy coating compared with uncoated azacitidine due to hydrolysis



PharmaShell® – Biologics - coated peptides for long acting formulations

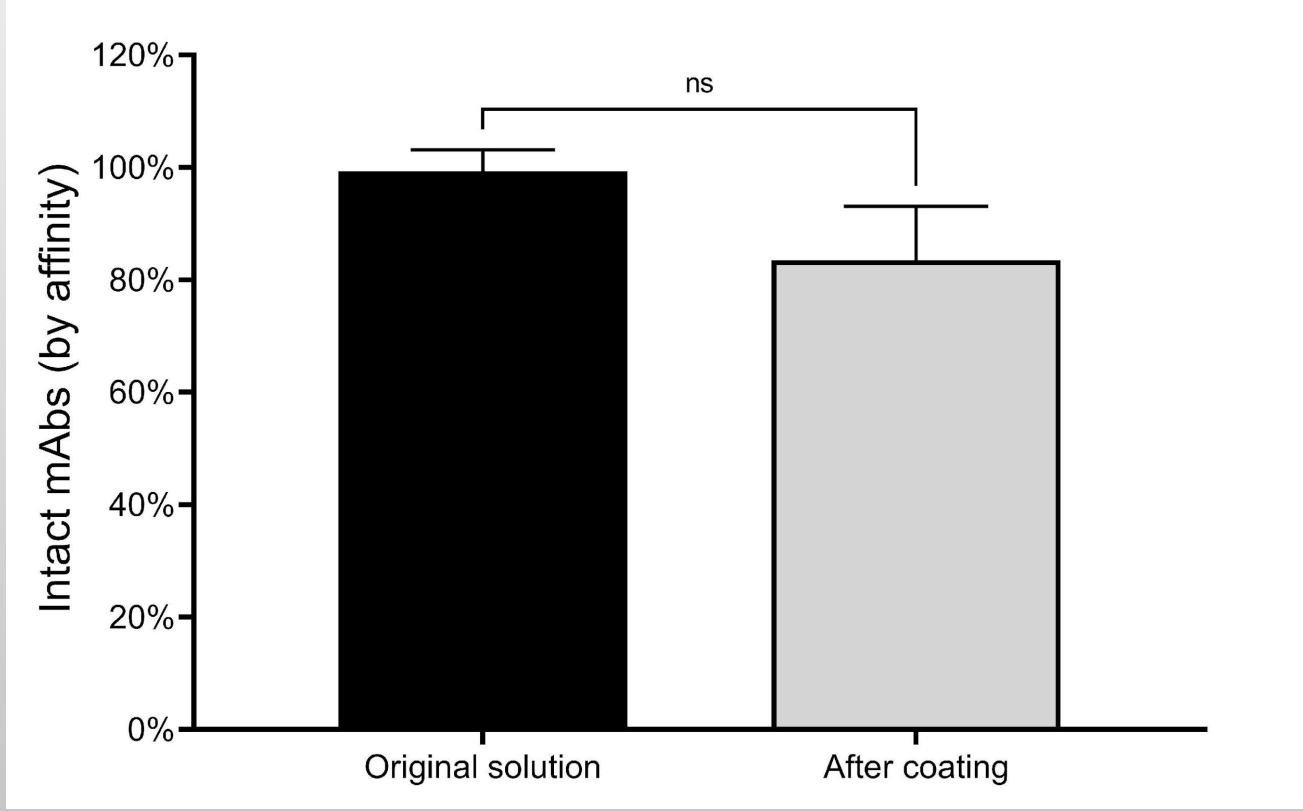
- **Water soluble peptides coated with PharmaShell®**
- **High drug load, >70% peptide**

- ***In vivo* release studied in mice**
  - Rapid clearance of uncoated peptide
  - Release of PharmaShell coated peptide
    - Small and controlled initial burst release, < 10%
    - Drug release for full duration of studies, 8 days

PharmaShell® Biologics: coated mAbs for long acting formulations

Affinity maintained after coating

- **A solution containing the monoclonal antibody ATH3G10 in Gly-Ac buffered saline was prepared for coating**
  - Dialysis to reduce sodium chloride and add stabilizer for drying (trehalose)
  - Spray-drying of the modified solution
  - PharmaShell-coating of the spray-dried particles
- **Affinity to the antigen was measured through enzymatic ligation assay (ELISA) and compared between processing steps**
- **Coated mAb was not significantly different from unprocessed mAb**



Error bars: standard deviation (n = 2–6, tech. rep.).
ns: p > 0.05 after unpaired two-sided t-test

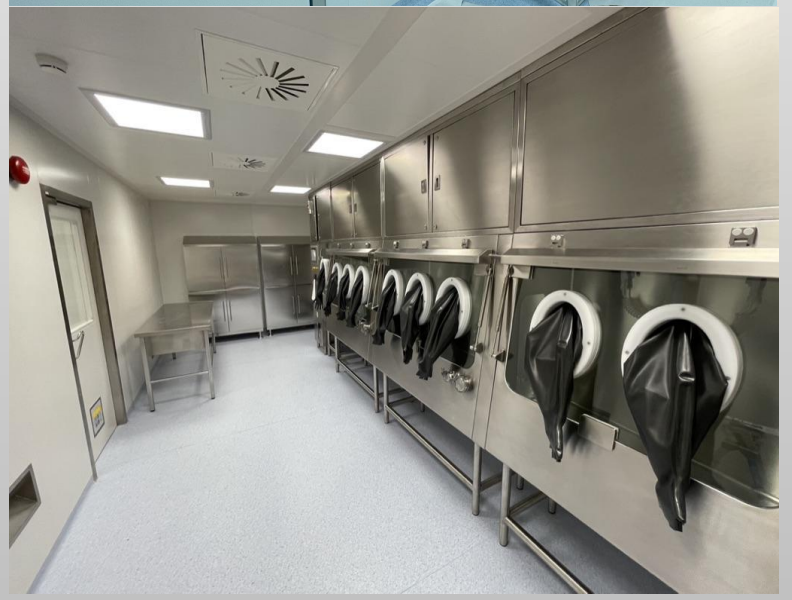
Sterilization of PharmaShell® coated material

- **Terminal sterilization**
  - Gamma irradiation at 25 kGy validated for NEX-18 (PharmaShell® coated azacitidine).
    - More information at Tech session 4 at 3pm today: Joel Hellrup, PhD

- **Aseptic processing**
  - Aseptic processing capability in Nanexa´s Pilot plant facilities
    - APIs that do not tolerate gamma irradiation

Nanexa's pilot plant with capacity to support projects through clinical development in phases I-III

- State-of-the-art GMP-pilot plant with unique possibilities
  - Manufacturing of PharmaShell® in kg-scale through collaboration with Applied Materials Inc.
  - Built with isolator technology for handling of highly potent(OEL-5) pharmaceuticals, like cytostatic compounds
  - Prepared for aseptic production (e.g. biologics, peptides, proteins, antibodies)
- Relocation to new facilities during Q2 2022
  - 900 sqm pilot plant, labs and offices
- New facilities inspected by Swedish MPA June, and GMP certificate expected to be in place September 2022

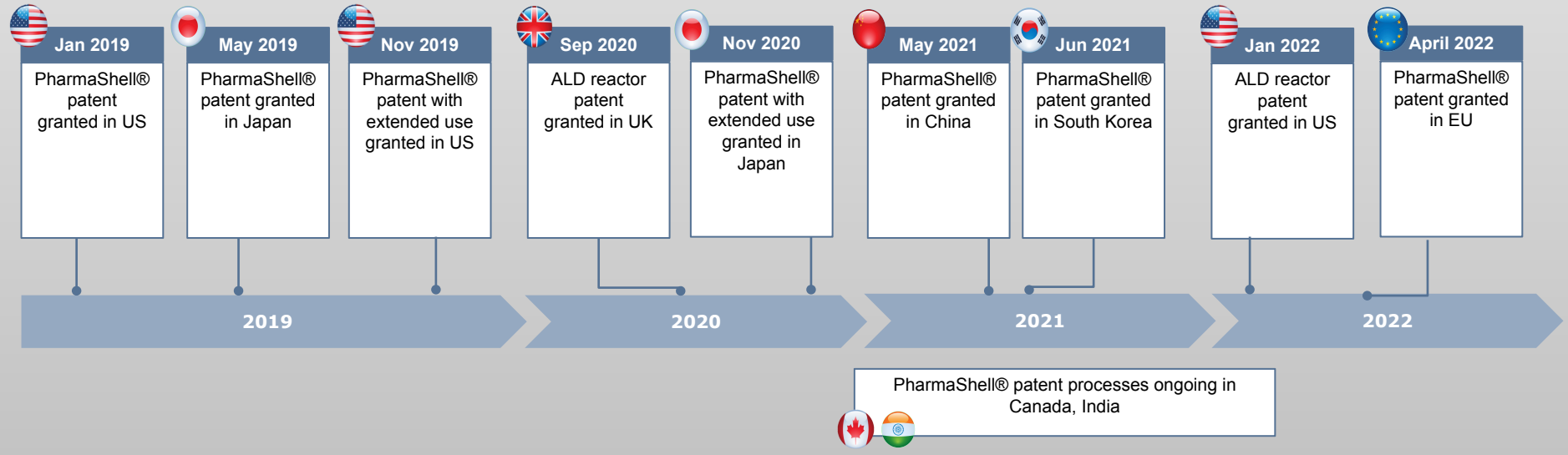


PharmaShell® patent portfolio

Long term strategy to build strong patent portfolio to enable consistent value growth

- Covering particle generation, ALD processing and product formulation
- Patent protection from first approved patent until 2033
- Ongoing processes with applications pending for the PharmaShell base patent in additional countries
- Several other patent applications pending

Patent strategy covering all major markets



Thank you for listening !

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