PharmaCytics

From needle to pill

Trick the Guts!

Company Profile

Company Bio

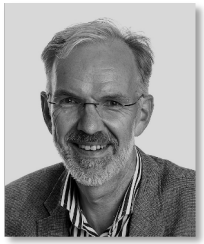
Start Of Operations	May 2015
Offices	Pivot Park (Oss) and Nijmegen, NL
FTE Count	10.0 (8 chemists of which 4 PhD's)
Focus Area	parenteral drugs into oral drugs

Stage of Development

Clinical Milestones Reached	✓ Developed unique chemistry ✓ PoC; increased bio-availability ✓ Compounds showed 5-10x impr. ✓ Pipeline Development ✓ Toolbox of 22 linkers 6 nutrients allowing a **tailor made** approach
Commercial Milestones Reached	✓ 2 partnerships with 2 big pharma

Leadership Team

Gerrit Veeneman (PhD)
CSO and co-founder
- 25+ years of drug dev. experience
- Former research lead Organon, >120 publications, >12 patents filed
- Highly experienced in drug delivery and prodrug technologies



Han van 't Klooster
CEO and co-founder
- 25+ years of industry experience
- Former GM Benelux Pharmion, MT-member EU/ROW Chiron
- Strong infrastructure builder and broad pharma network

General Advisory Board

Advisory Board – Disease specific

Addressable Issue

Unmet need: Poor drug-like features of compounds

Resolving the pharmacokinetic (PK) shortcomings of drugs

A significant part of current oral compounds suffers from poor PK

→ 20-30% of marketed drugs

- Requirement for higher dosing increases (GI-) side-effects
- Limited efficacy and high inter-patient variability
- Suboptimal route of administration (parenteral vs oral) leading to lower compliance rates

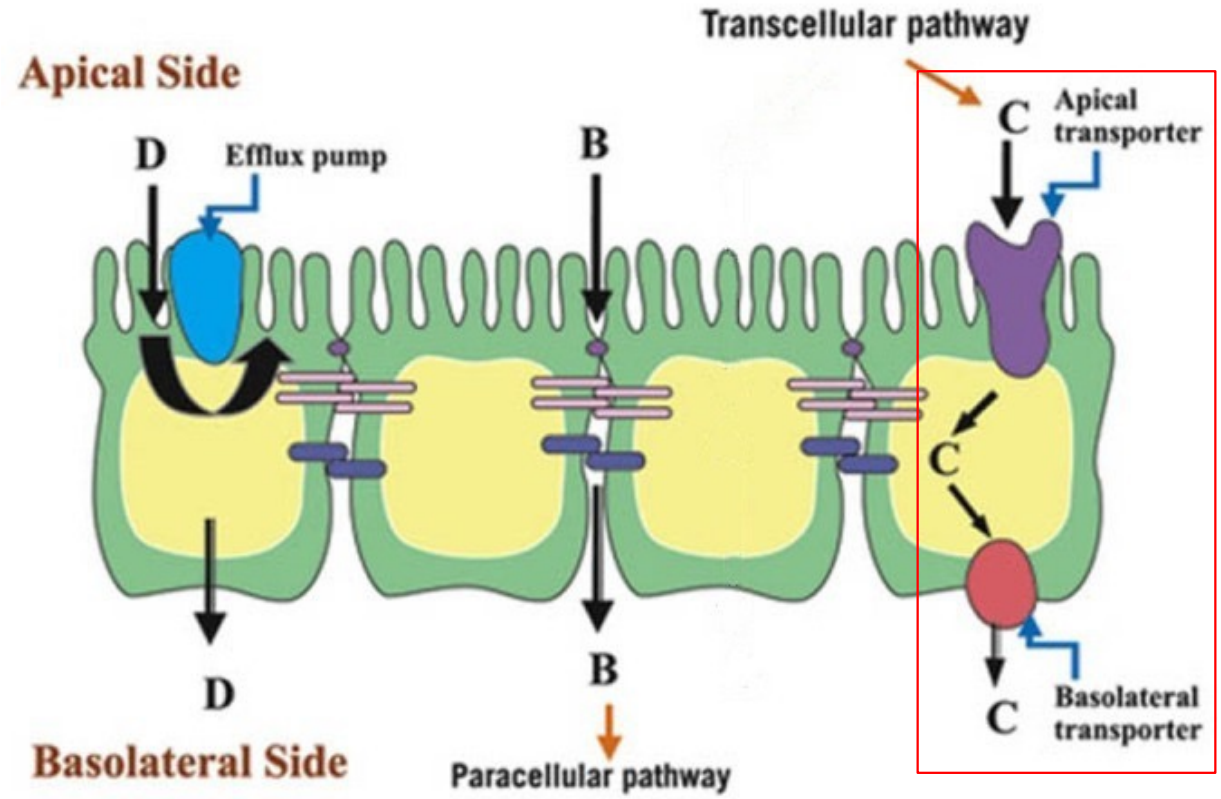
→ 70% of drug candidates in pipeline

- High attrition of drug candidates in drug development process

Prodrugs: making non-optimal drugs better

- Current solutions are often focused on conventional methods to improve formulation or employ micronizing techniques
- Prodrugs are proven to be one of the most encouraging solutions for optimal drug delivery
- Existing prodrugs solutions have ample room for improvement (e.g. low control over compound, addressing single issues, complex scientific process)
- PharmaCytics' proprietary NDCt provides a new look and solutions to these issues

Nutrients can make use of specific nutrient transporters in the small intestines



Old fashioned drugs take route D or B
i.e. through the intestinal wall
or tight junction;
That is passive and inefficient.

Nutrients go by multigrams through route C

Can we make drugs look like nutrients?

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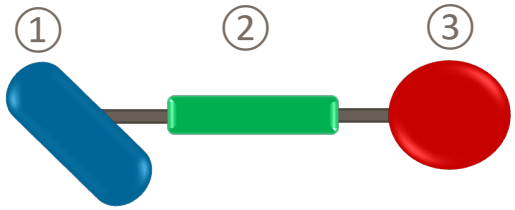
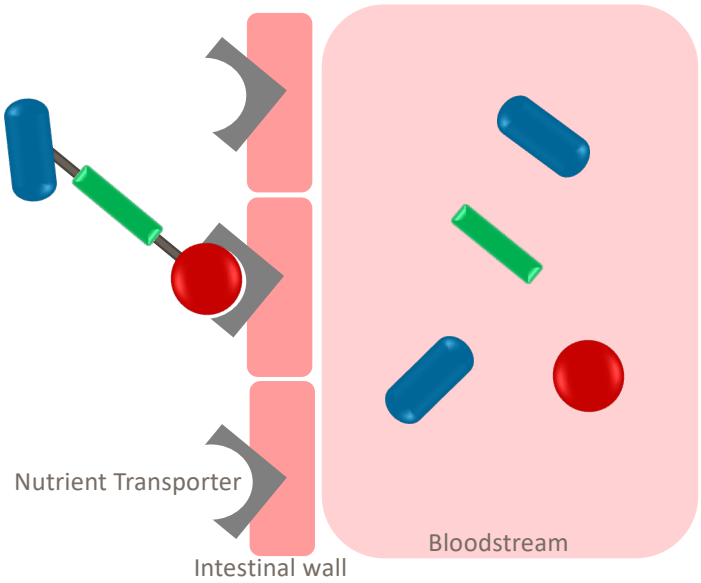
Our *Unique* Technology

Nutrient Drug Conjugate (NDCt) Design



1. Drug: NDCt can be applied to multiple functional groups (e.g. amine, thiol, hydroxy, carboxyl)
2. Linker: Facilitates synthesis and transport
3. Nutrient mimic: Transporter substrate and enhances solubility

Mechanism of Action



Linkers can potentially be used for any purpose

- Attachment nutrients to drugs
- Attachment drugs to proteins
- Attachment drugs to other drugs (codrugs)

NDCt exploits specific nutrient transporters in small intestines (as opposed to inefficient passive transport)

PharmaCytics has developed a unique prodrug technology in which drugs are linked to nutrients in such a way that the resulting conjugate is recognized and transported by the nutrient-transporters in the gut wall. Our platform technology can address the **full spectrum of issues around oral bioavailability** and provides **high control over the compound**

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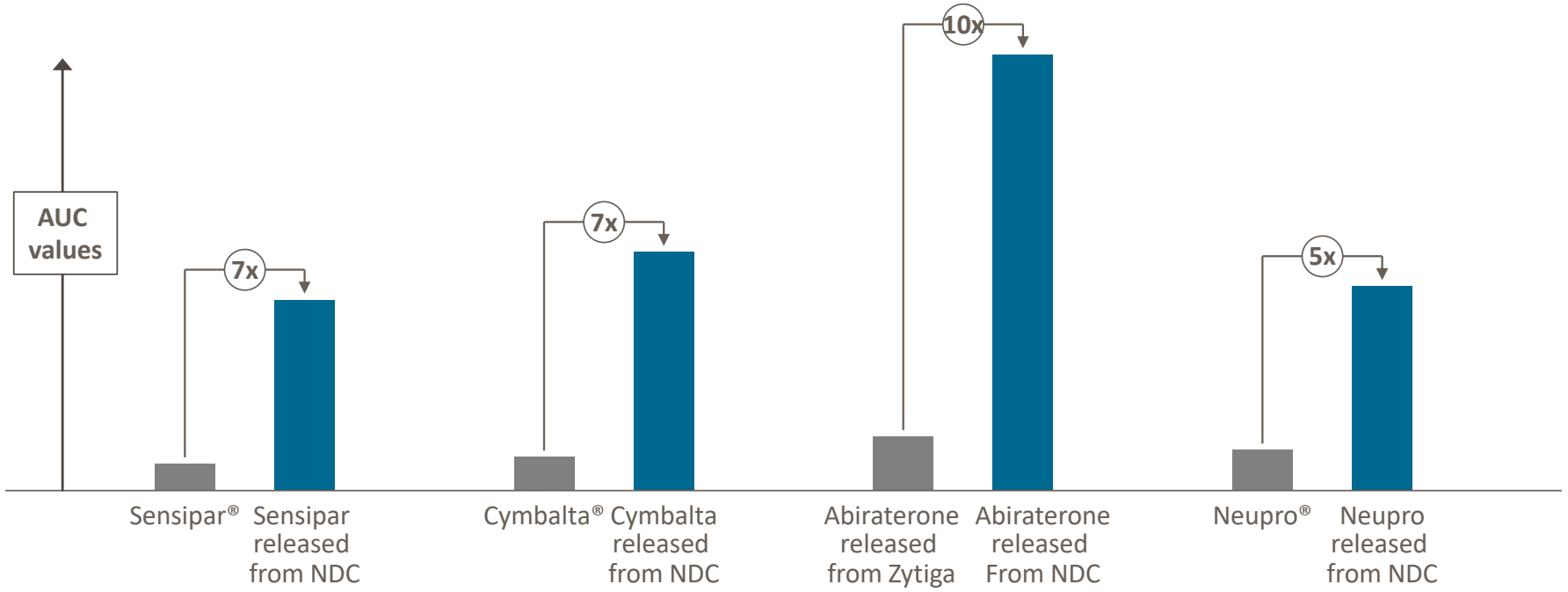
Proof of Concept in 4 examples - applicable to 100's

Unprecedented *gain in oral bioavailability*



Notes:

- Preclinical studies in Beagle dogs
- Neupro® marketed in parenteral formulation

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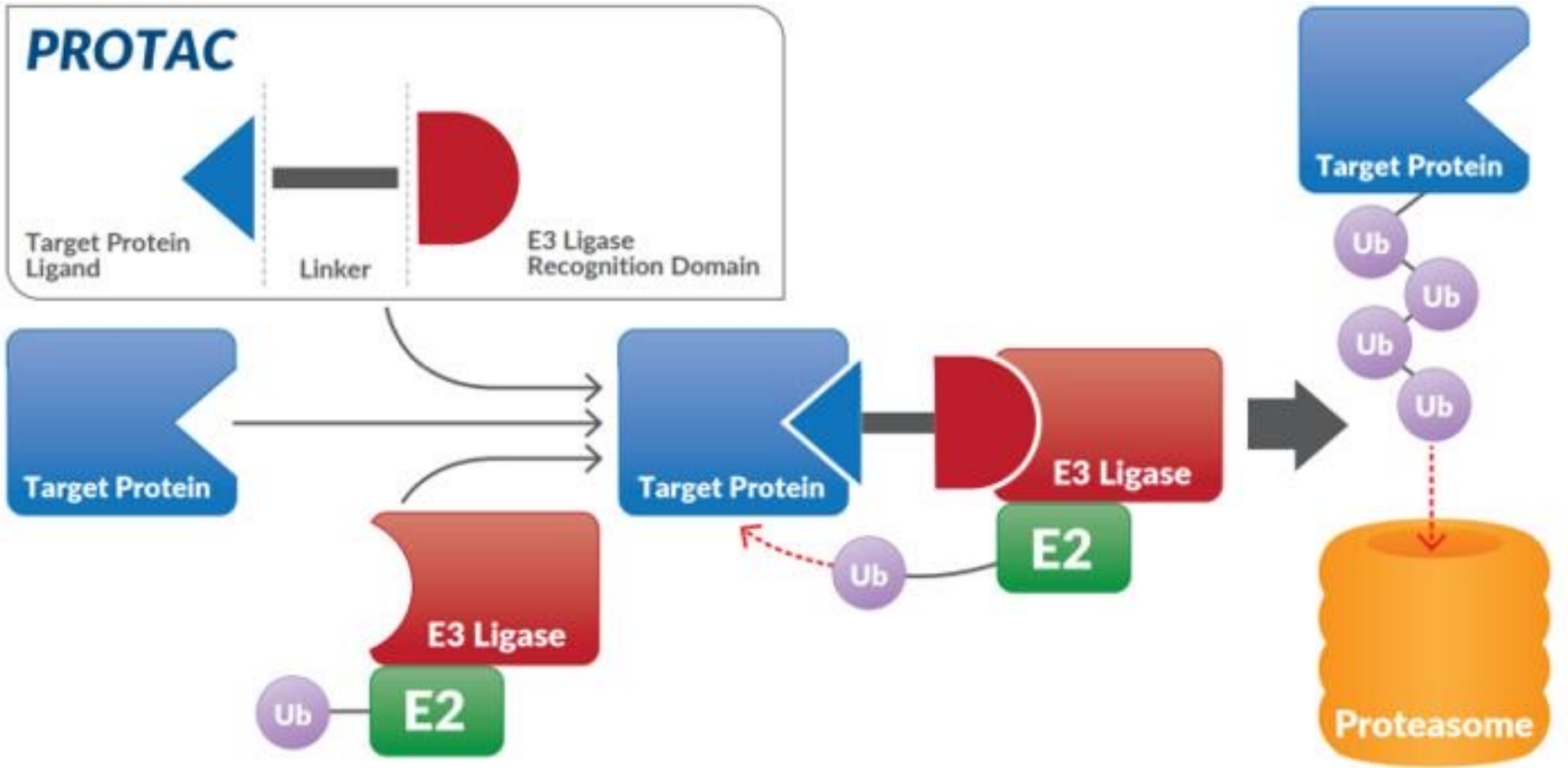
Pipeline focus: PROTAC *in action*



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Differences between an inhibitor and a PROTAC

	Inhibitor	PROTAC
Action	Blocks function of protein	Destroys protein
Effect	Inhibition, but equilibrium: not possible to inhibit for 100%	Degradation; it takes time and energy for cells to resynthesize protein
Efficiency	One molecule inhibits one protein molecule	PROTAC can destroy more protein molecules
Mutations	Inhibitor works less or not anymore	Little influence as long as inhibitor still binds
Administration	Frequently oral	Intravenous

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Current situation

- All Pharma companies are now actively involved with PROTACs
- Great demand for technology to convert PROTACs into oral formulation
- PC has knowledge and building up experience with PROTACs with propriety project and collaboration project
- NDC technology looks very applicable to PROTACs:
  - Presence of suitable functional groups
  - Molecular weight ~1000-1500
  - PROTACs are reasonable stable

- 15 PROTACs in clinical trials (2020-2021); one claimed to be oral
- Structures not made public

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