Ascendis Pharma A/S

Virtual Oncology R&D Day

November 20, 2020

Cautionary Note On Forward-Looking Statements

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, such as statements regarding our future results of operations and financial position, including our business strategy, prospective products, availability of funding, clinical trial results, product approvals and regulatory pathways, collaborations, licensing or other arrangements, the scope, progress, results and costs of developing our product candidates or any other future product candidates, the potential market size and size of the potential patient populations for our product candidates, timing and likelihood of success, plans and objectives of management for future operations, the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, and future results of current and anticipated products, are forward-looking statements. These forward-looking statements are based on our current expectations and beliefs, as well as assumptions concerning future events. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the results discussed in the forward-looking statements. These risks, uncertainties and other factors are more fully described in our reports filed with or submitted to the Securities and Exchange Commission, including, without limitation, our most recent Annual Report on Form 20-F filed with the SEC on April 3, 2020 particularly in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations”. In light of the significant uncertainties in our forward-looking statements, you should not place undue reliance on these statements or regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

Any forward-looking statement made by us in this presentation speaks only as of the date of this presentation and represents our estimates and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation to update these statements publicly, whether as a result of new information, future events, changed circumstances or otherwise after the date of this presentation.

This presentation concerns product candidates that are or have been under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration, European Medicines Agency or other foreign regulatory authorities. These product candidates are currently limited by U.S. Federal law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated.

Virtual Oncology R&D Day Agenda

9:00 a.m.

Welcome & Agenda Overview
Scott T. Smith, *SVP, CFO*

9:01-9:05 a.m.

Vision 3x3
Jan Møller Mikkelsen, *President & CEO*

9:05-9:20 a.m.

TransCon™ Platform & Product Innovation
Kennett Sprogøe, Ph.D., *SVP, Head of Innovation and Research*

9:20-10:00 a.m.

TransCon TLR7/8 Agonist & TransCon IL-2 β/γ
Juha Punnonen, M.D., Ph.D., *SVP, Head of Oncology*

Stina Singel, M.D., Ph.D., *Head of Clinical Development, Oncology*

10:00-10:30 a.m.

Q&A

Vision 3x3

Jan Møller Mikkelsen
President & CEO

Company Overview

- Create best-in-class products addressing unmet medical needs by applying TransCon™ technologies to parent drugs with clinical proof-of-concept
- Endocrinology rare disease
  - TransCon hGH: pediatric GHD BLA (PDUFA June 25, 2021) and MAA submitted; adult GHD phase 3 trial ongoing
  - TransCon PTH: Submitted US, Canadian and European regulatory filings to initiate adult HP phase 3 trial
  - TransCon CNP: Phase 2 ACcomplisH ongoing and ACcomplisH China Trial[1] initiated for achondroplasia
  - Build leading market positions for each product candidate with commercial focus on maximizing global reach
  - Strategic investment in VISEN Pharmaceuticals for endocrinology rare disease products in China
- Oncology
  - First IND filing expected for TransCon TLR7/8 Agonist by year-end 2020
  - TransCon IL-2 β/γ IND filing or similar expected in Q3 2021
- As of September 30, 2020, cash, cash equivalents and marketable securities of €957.5 million

[1]Through VISEN Pharmaceuticals

Vision 3x3: Building a Leading BioPharma Company

Our Goal is to Achieve Sustainable Growth through Multiple Approaches

- Obtain regulatory approval for three independent Endocrinology Rare Disease products
  - TransCon Growth Hormone for pediatric growth hormone deficiency
  - TransCon PTH for adult hypoparathyroidism
  - TransCon CNP for achondroplasia
- Grow Endocrinology Rare Disease pipeline through
  - Global clinical reach
  - Pursuing 9 total indications, label optimization, and life cycle management
  - New endocrinology products
- Establish global commercial presence for our Endocrinology Rare Disease area
  - Build integrated commercial organization in North America and select European countries
  - Establish global commercial presence through partners with local expertise and infrastructure
- Advance a high value oncology pipeline with one IND or similar filing each year
- Create a third independent therapeutic area with a diversified pipeline

TransCon Technology Platform & Product Innovation

Kennett Sprogøe, Ph.D.
SVP, Head of Innovation and Research

The Evolution of TransCon Technology

Vision of Ascendis Founding Scientists

Precise release of active drug, from a prodrug, without changing the molecule's biology

The Historical Challenge

Conventional technologies (protein enlargement and encapsulation) are associated with altered biology and unpredictable drug release

The Revolutionary Solution

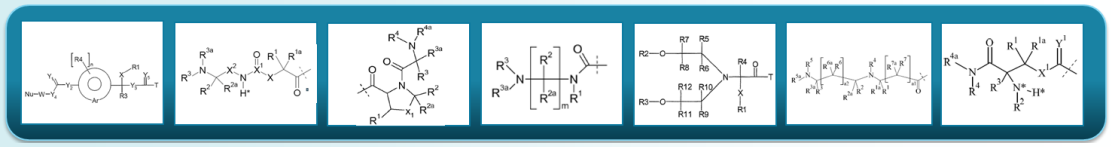
To combine prodrug and predictable release technologies into one platform to ensure tailored delivery of unmodified drug

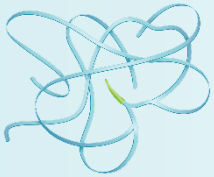
TransCon technology reversibly conjugates a drug to a carrier and predictably releases the unmodified drug under physiological conditions

*Trans*ient *Con*jugation: A Powerful, Flexible Platform

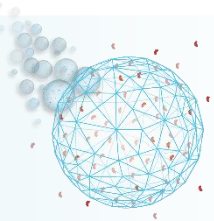
TransCon Prodrug: 3 components

- TransCon Linker
- TransCon Carrier
- Parent Drug





Soluble Carriers



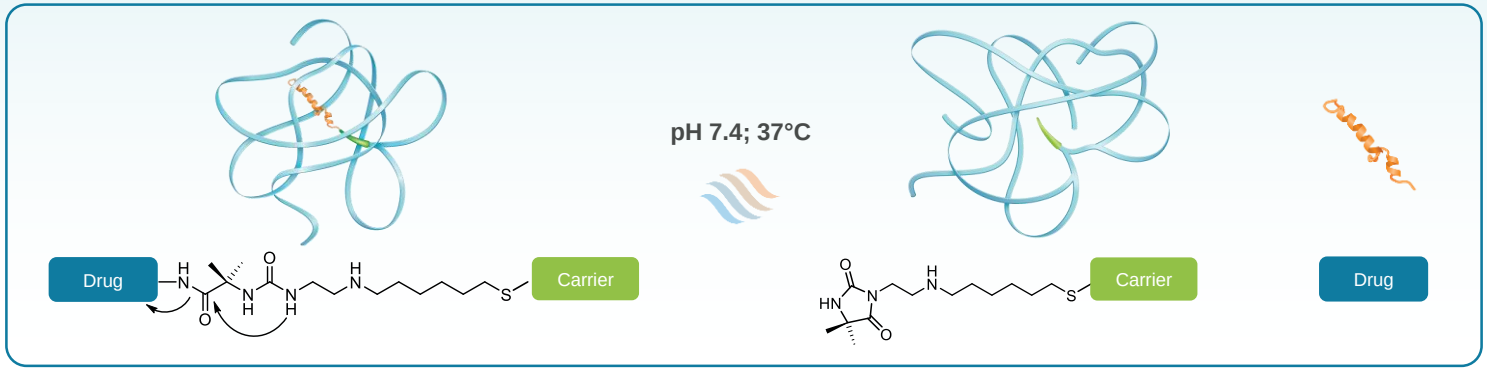
Insoluble Carriers

Antibodies, Antibody Fragments, Proteins, Peptides and Small Molecules

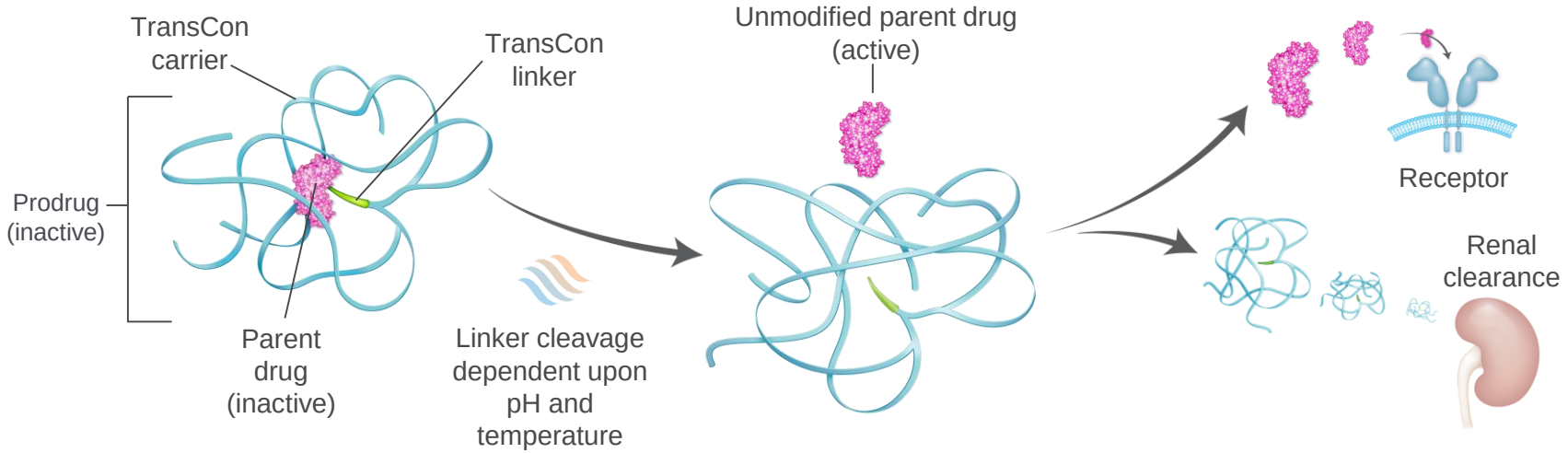
ascendis pharma

TransCon Technology: The TransCon Linker

- Cleaves in an enzyme-independent fashion, ensuring reproducible drug release; *in vitro* to *in vivo* correlation with high predictability
- TransCon linkers remain covalently bound to the carrier molecule after release of the unmodified parent drug
- Enables tunable design of prodrugs with dosing frequency from daily up to six months or more



TransCon Technology: Sustained Systemic Release

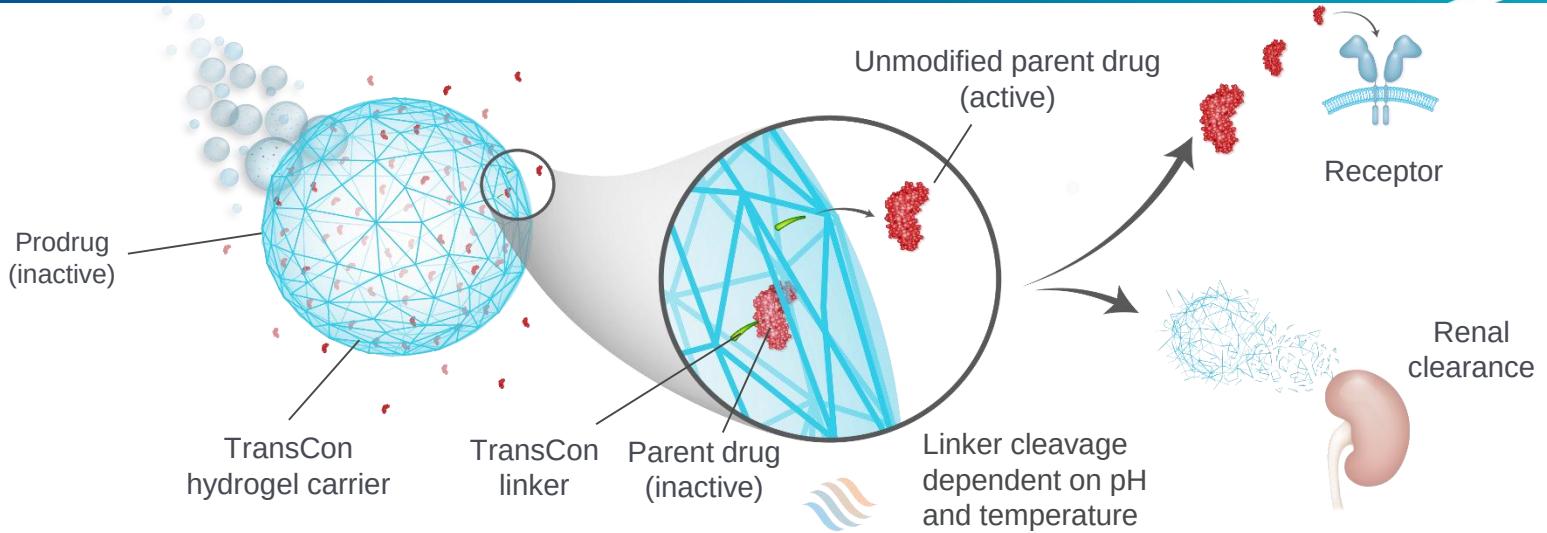


Parent drug is transiently bound to a TransCon linker-soluble carrier moiety, which inactivates and shields parent drug from clearance

Following injection, the linker is designed to autocleave at a specific rate to predictably release unmodified parent drug

Designed to distribute released molecule like the parent drug; linker-carrier is cleared renally

TransCon Technology: Sustained Localized Release



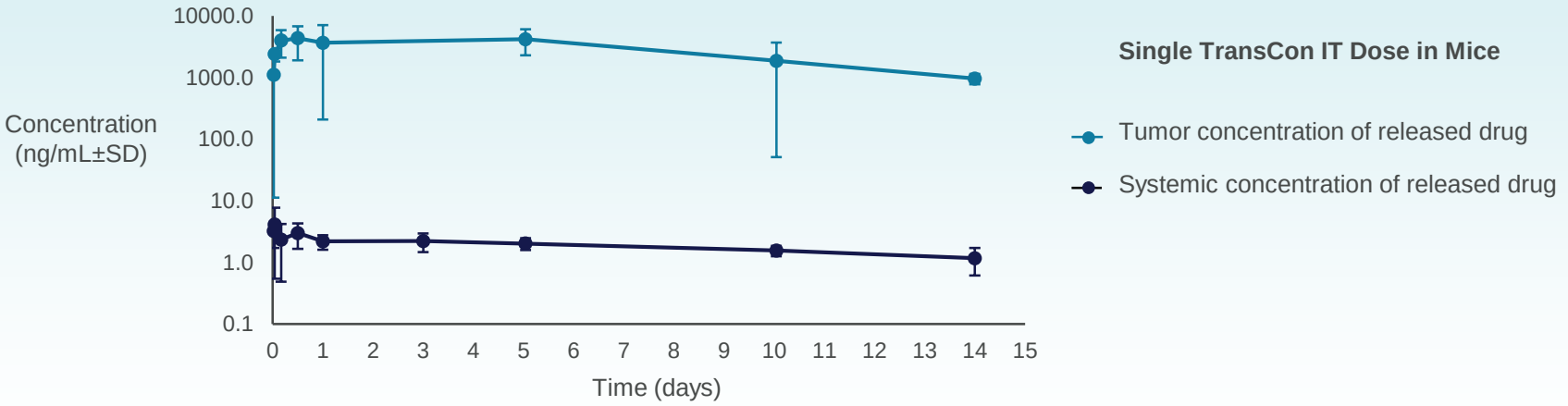
Parent drug is transiently bound to TransCon linker-hydrogel carrier, which inactivates, shields parent drug and prevents clearance

Following injection, the linker is designed to autocleave at a specific rate to predictably release unmodified parent drug

Designed to provide sustained high local drug levels with low systemic exposure; hydrogel degrades into small polymers that are renally cleared

TransCon IT: Potential Paradigm Shift in Intratumoral Delivery

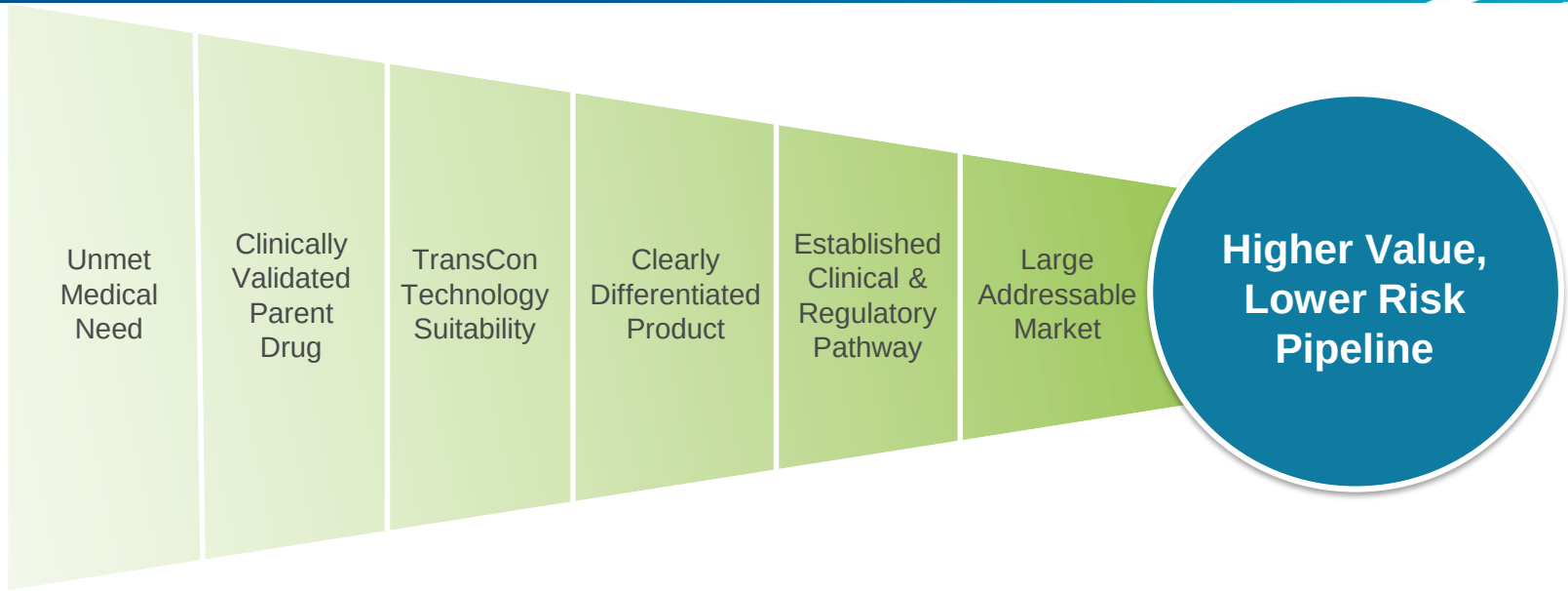
TransCon Intratumoral (IT) addresses the problems of conventional IT administration including rapid clearance from the tumor, high systemic exposure and toxicity



TransCon IT is designed to stay in the tumor and slowly release the drug ensuring high tumor drug concentration and low systemic exposure

Data on file.

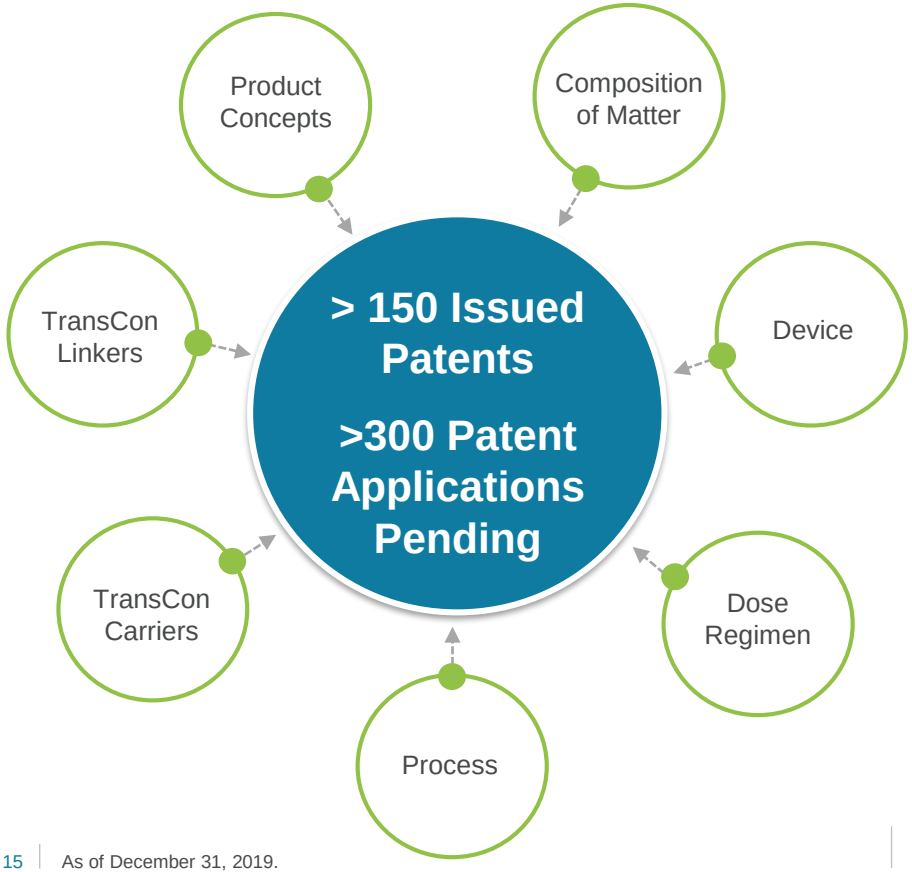
Algorithm Used in Endocrinology Used to Build Oncology Pipeline



Our unique algorithm for product innovation has resulted in clinical validation of 3 out of 3 product candidates in endocrinology rare diseases

We are continuing to apply our algorithm to build a pipeline in oncology and are committed to entering a 3rd therapeutic area

TransCon Enables Multi-level Patent Protection



- TransCon prodrugs eligible for new composition of matter IP
  - TransCon prodrugs are new chemical entities
  - Enables new patent life for prodrugs of parent drugs
- A multi-layered patent strategy is applied to protect our assets

As of December 31, 2019.

TransCon: An Innovative Technology Platform

- TransCon technologies combine the benefits from prodrug and predictable release technologies with the known biology of the parent drug
- Technology validated within endocrinology with a high success rate in multiple clinical programs; TransCon hGH BLA/MAA filed
- Building on the success in endocrinology, we apply our algorithm for product innovation to help select our oncology pipeline
- Developed an intratumoral platform that aims to transform IT administration of small molecules, peptides, proteins, antibody fragments and antibodies
- TransCon prodrugs are new chemical entities eligible for new composition of matter IP

Our vision is to leverage TransCon technologies to turn the body's immune system into the therapeutic – to improve patient outcomes

Oncology

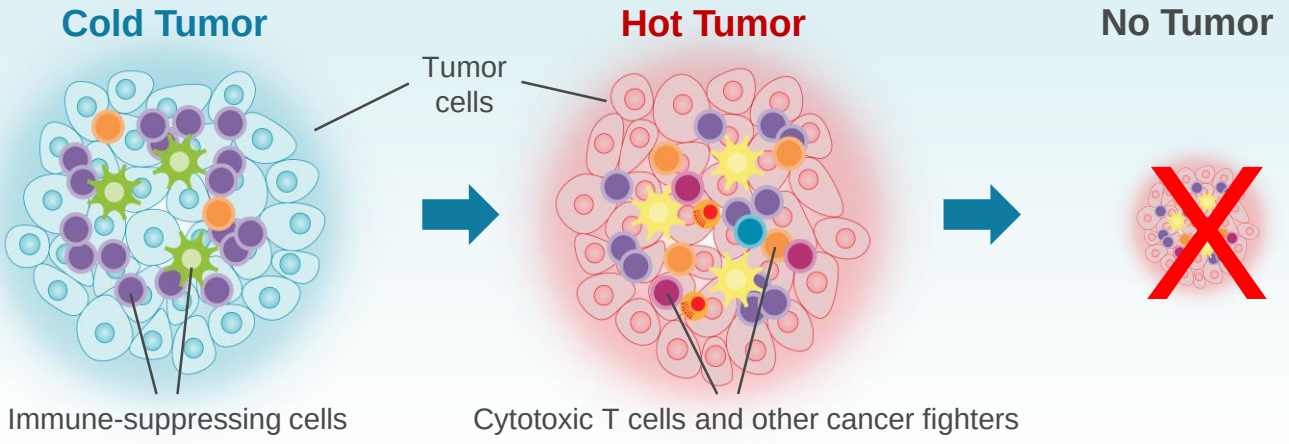
Juha Punnonen, M.D., Ph.D.
SVP, Head of Oncology

Stina Singel, M.D., Ph.D.
Head of Clinical Development, Oncology

TransCon Positioned to Transform Cancer Therapy

TransCon systemic and IT therapies designed to enhance anti-tumor responses by

- Providing sustained modulation of tumor microenvironments
- Activating cytotoxic immune cells



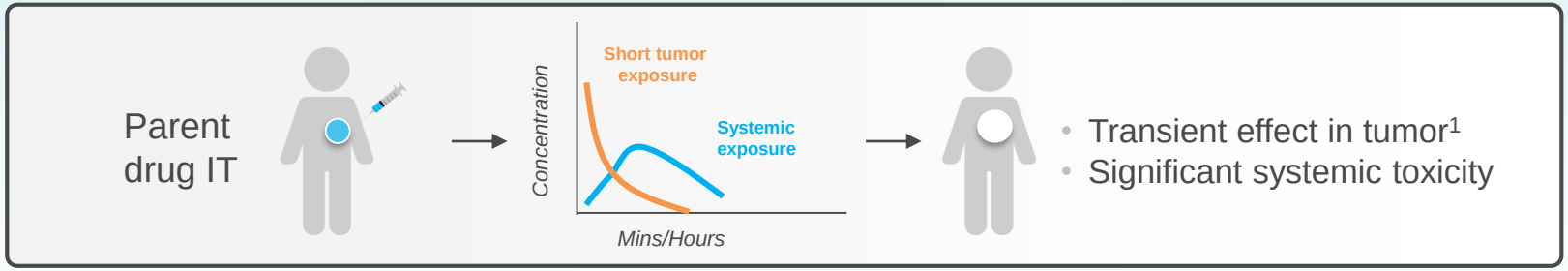
Applicable for diverse drug classes and mechanisms of action; opportunity for combination approaches

Oncology Portfolio Strategy

- Create best-in-class oncology therapies by applying TransCon systemic and IT technologies to parent drugs addressing clinically validated pathways
- Improve outcomes with parent drugs that are currently limited by suboptimal efficacy and systemic toxicity
  - Apply Ascendis' unique algorithm for product innovation to oncology development
- Build a diversified high-value pipeline addressing multiple indications
  - Two near-term IND candidates with potential synergistic combination effects
- Enable rapid path to global commercialization

Intratumoral Treatment Has Been Challenging

- Treatment of cancer via IT administration of oncolytic virus has achieved clinical proof of concept with talimogene laherparepvec (T-VEC) in advanced melanoma
- However, conventional IT treatments face major challenges due to short tumor exposures[1], high systemic Cmax and need for frequent dosing



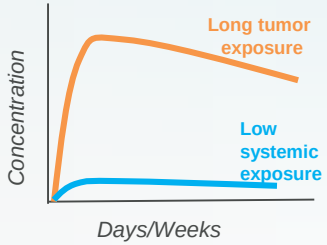
TransCon technology has the potential to overcome the limitations of conventional intratumoral treatments

1 Example: STING agonist "plasma half-life ranging from 8 to 28 min"
Meric-Bernstam F, et al. ASCO annual meeting, 2019; Oral presentation: Abstract 2507.

TransCon IT Aims to Transform Intratumoral Treatments

- Slow IT release allows for potential activity in tumor and draining lymph nodes for weeks or months, while keeping systemic exposure minimal
- Designed to enable new multi-agent combinations without added toxicity
- Potential for long dosing interval enabling treatments of hard-to-access tumors

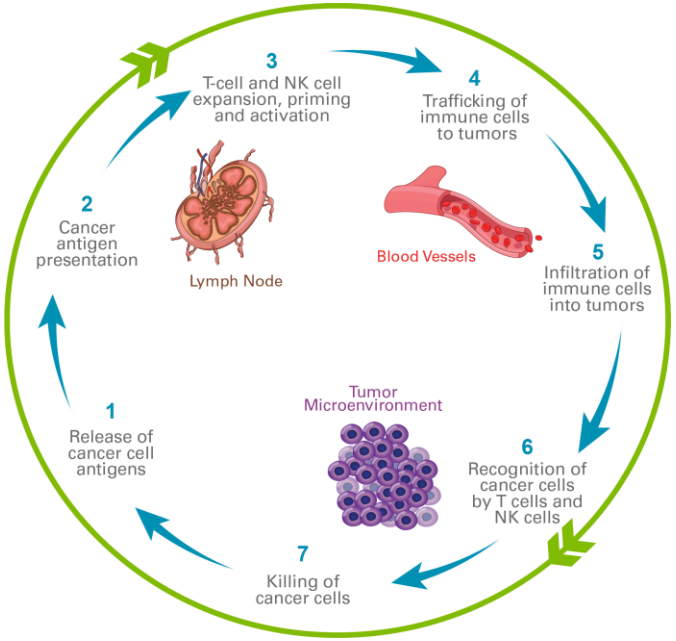
TransCon IT



- Sustained potent activity in the tumor
- Minimized systemic toxicity

TransCon technology provides potential for sustained modulation of tumor microenvironments with infrequent dosing and minimized systemic toxicity

Two Near-term IND Candidates - Potential to Expand Pipeline to Address All Steps of the Immunity Cycle



TransCon TLR7/8 Agonist

Designed to activate antigen-presenting cells and enhance antigen presentation and, thereby, promote activation of cytotoxic immune cells (steps 2 and 6).

TransCon IL-2 β/γ

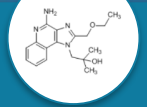
Designed to aid T cell and NK cell expansion, priming and activation as well as infiltration of immune cells in tumors (steps 3 and 5).

Additional TransCon Candidates in Preclinical Research

TransCon product candidates using systemic and IT approaches have the potential to affect all steps in the immunity cycle.

Combination approaches enable impact on all critical steps of anti-tumor response

Product Candidates in Oncology



TransCon TLR7/8 Agonist

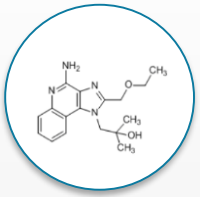
Opportunity for TransCon TLR7/8 Agonist in Solid Tumors

Efficacy
- Each injection designed to provide sustained exposure in the tumor for months to enhance immune activation
- Reduce risk of reaching super-high “ablative”, non-immunogenic levels

Safety
- Low systemic toxicity expected to reduce dose-limiting adverse events
- Infrequent dosing designed to improve practicality and reduce injection-related complications

Broad application
- Essentially all solid tumors are accessible for injection

TransCon TLR7/8 Agonist

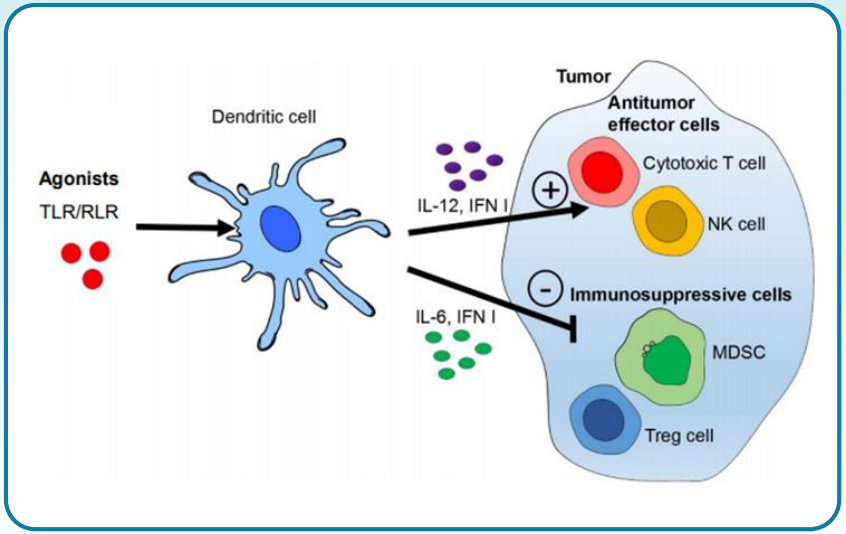


Designed for intratumoral, sustained release with ***minimal systemic exposure*** aiming for ***superior efficacy***

TLRs: Innate Immune Sensors of “Danger” Associated with Pathogens or Cell Death

Toll-like receptors (TLRs):

- Receptors for Pathogen- or Danger- (cell death) Associated Molecular Patterns
- Activate innate immunity, antigen presenting cells (APCs) in particular
  - Results in priming and expansion of cytolytic and helper T cells
- Inhibit suppressive mechanisms limiting anti-tumor responses

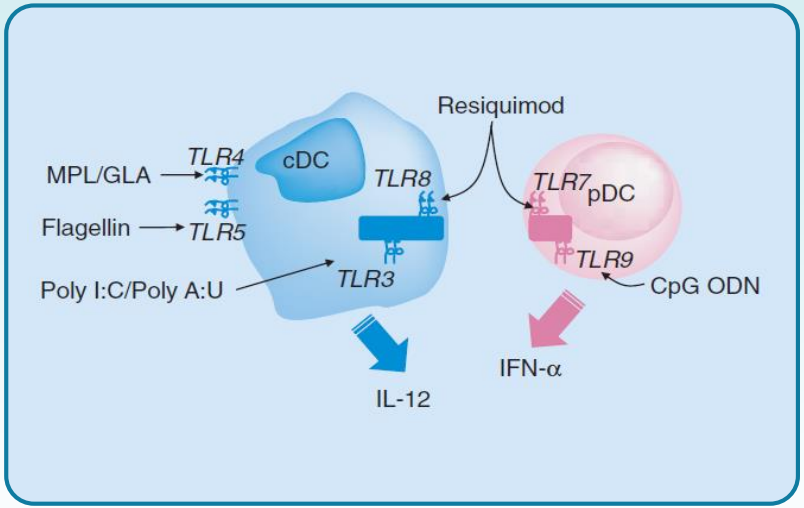


TLRs activate several key pathways critical in host defense against tumors

Bourquin C, et al. *Pharmacol Res*, 2020; 154:104192.

Resiquimod: TLR7/8 Agonist[1,2]

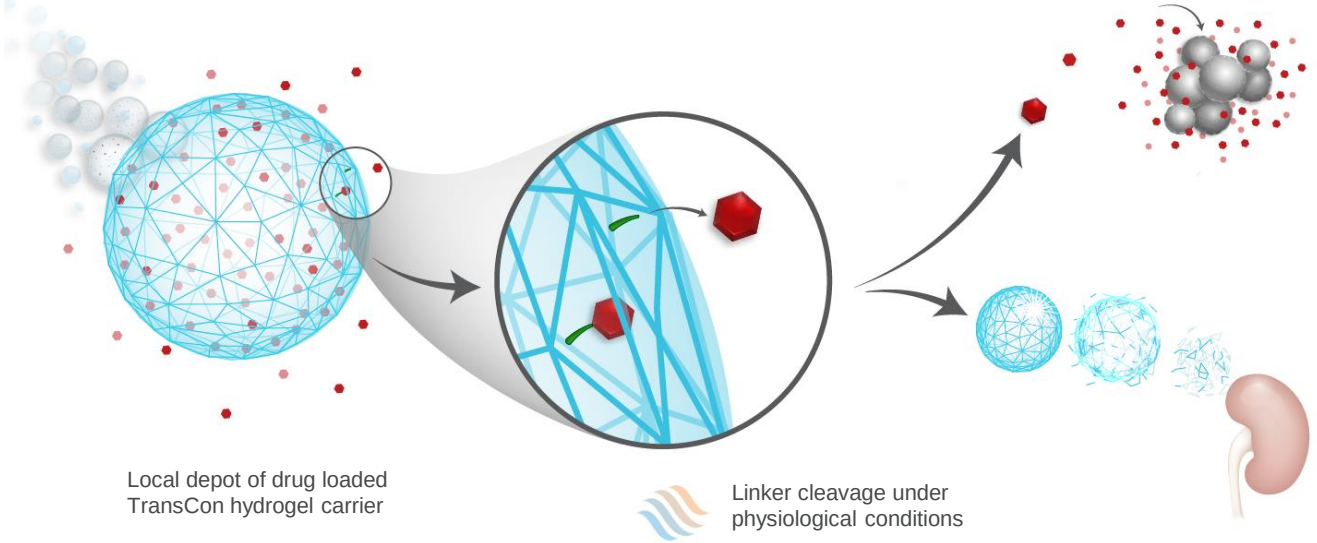
- Small molecule agonist of both TLR7 and TLR8
  - TLR7: mainly expressed in plasmacytoid dendritic cells (pDCs), to some extent in B cells, monocytes, macrophages and conventional dendritic cells (DCs)
  - TLR8: primarily expressed in conventional DCs, monocytes, macrophages and myeloid DCs
- Potent activator of the innate immunity
  - Elevates proinflammatory cytokines: IL-12, IFNs, TNF-α, IL-1, chemokines
  - Enhances antigen presentation: upregulated MHCII, costimulatory molecules (e.g. CD80/86)
  - Enhances anti-tumor immunity



Resiquimod activates both conventional DCs and pDCs

[1] Vasilakos J and Tomai M. *Exp Rev Vaccines*, 2013; 12:809-819.
[2] Rook A, et al. *Blood*. 2015;126(25):2765.

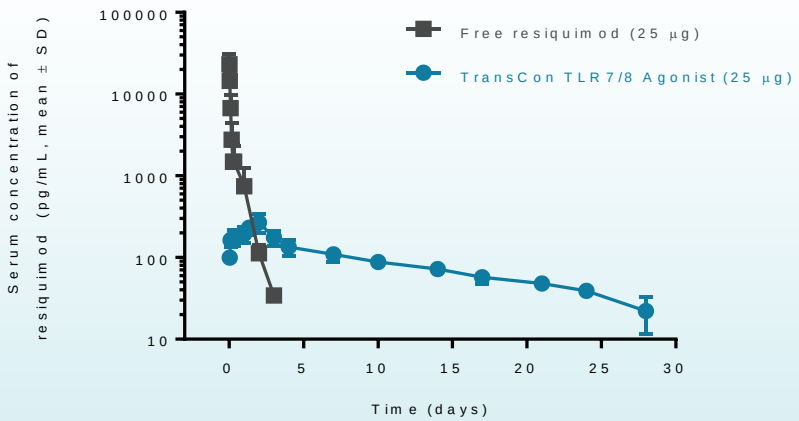
TransCon TLR7/8 Agonist: Sustained Intratumoral Release of Resiquimod



- Resiquimod transiently conjugated to TransCon hydrogel carrier, designed to provide sustained local release of unmodified resiquimod
- Designed to provide sustained activation of intratumoral APCs driving tumor antigen presentation and induction of immune stimulatory cytokines in the tumor

TransCon TLR7/8 Agonist Resulted in Sustained Release of Resiquimod over Several Weeks

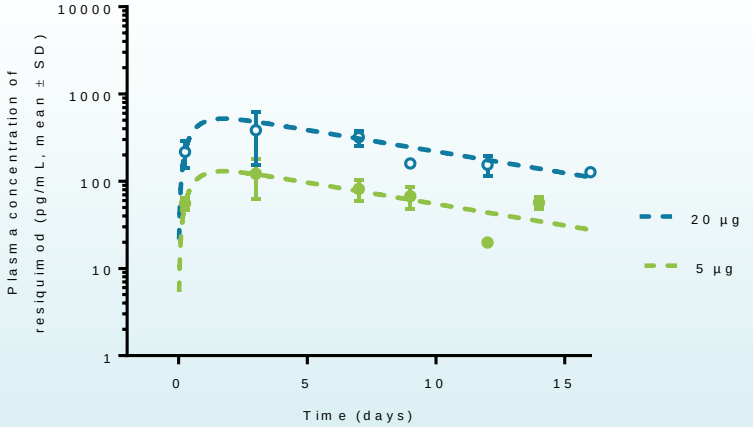
Subcutaneous administration in rats



Parent Drug (free resiquimod): $T_{1/2}$ = ~10 h

TransCon TLR7/8 Agonist: $T_{1/2}$ ~10 days

Intratumoral (CT26) administration in mice



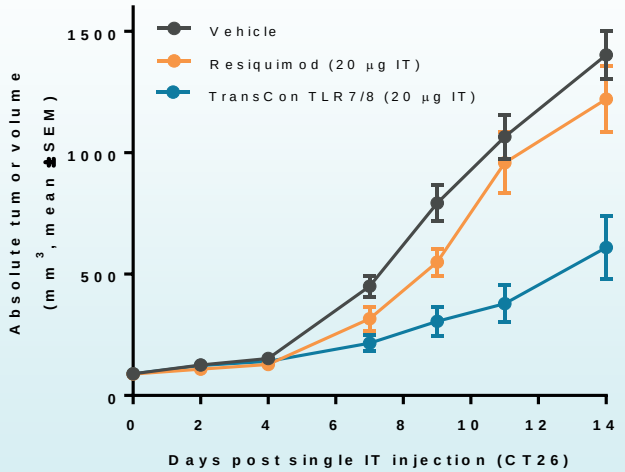
TransCon TLR7/8 Agonist: $T_{1/2}$ ~12 days

TransCon technology enables 25-fold increased half-life and avoids high Cmax

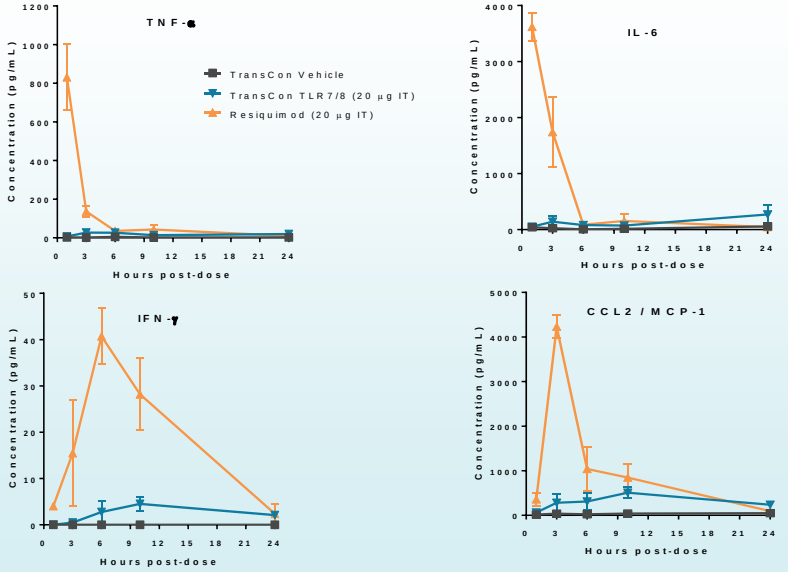
Zuniga L, et al. SITC annual meeting. 2019; Poster 676.

Potent Tumor-growth Inhibition with Low Systemic Cytokines

Single Dose TransCon TLR7/8 Agonist versus Comparable Dose of Resiquimod



Lower Systemic Cytokine Release by TransCon TLR7/8 Agonist than Comparable Dose of Resiquimod



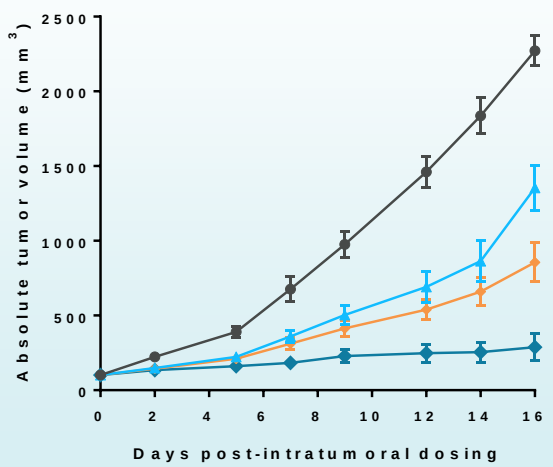
TransCon TLR7/8 Agonist has the potential to provide more potent anti-tumor benefits without dose-limiting toxicity, as IL-6 and TNF-α associate with cytokine release syndrome in patients[1,2]

[1] Gullo A, et al. *Front Biosci.* 2010; E2: 906-911.
[2] Norelli M, et al. *Nat Med.* 2018; 24(6):739-748.

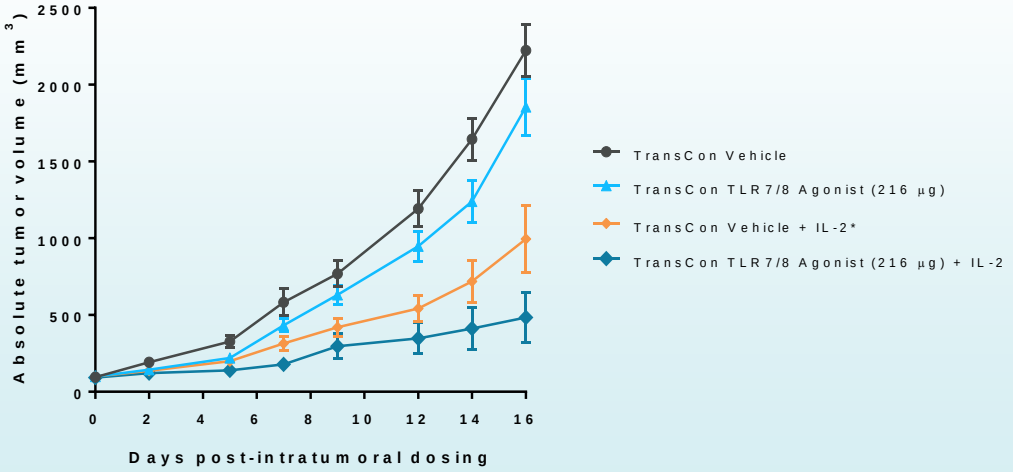
Single-dose of TransCon TLR7/8 Agonist Triggered Abscopal Anti-tumor Inhibition and Enhanced Anti-tumor Effects of IL-2

Single IT Dosing (CT26 tumor model)

Injected Tumor



Non-injected Tumor



TransCon TLR7/8 Agonist IND expected by year-end 2020

*IL-2 dosed at 20 µg twice daily on days 0-4, once daily on days 8-12.
Zuniga L, et al. SITC annual meeting. 2019; Poster 676.

Product Candidates in Oncology

IL-2 Selective for the IL-2Rβ/γ

TransCon
IL-2 β/γ

Interleukin-2 (IL-2): Validated Cytokine with Suboptimal Receptor Binding *and* PK Properties

Suboptimal receptor binding

- Two receptors: IL-2Rα/β/γ and IL-2Rβ/γ
- α/β/γ receptor activates Tregs and endothelial cells, reducing efficacy and increasing risk of capillary leak syndrome

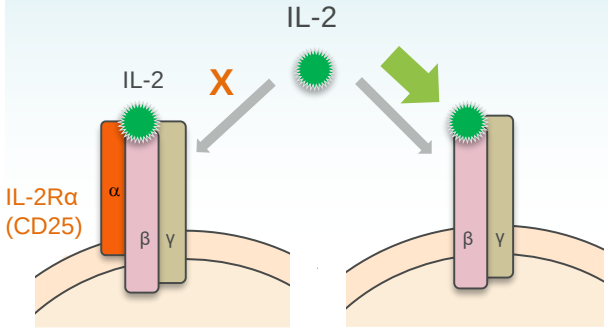
Suboptimal PK

- Short half life of IL-2 (~1.5 h)
- High Cmax and pulsatile dosing drive adverse events

- Several IL-2 approaches in development
- To our knowledge, none have fully solved both shortcomings of IL-2

Next Generation IL-2: Designed for Desired Receptor Binding and Exposure

1) Prevent IL-2Rα binding to selectively activate IL-2Rβ/γ



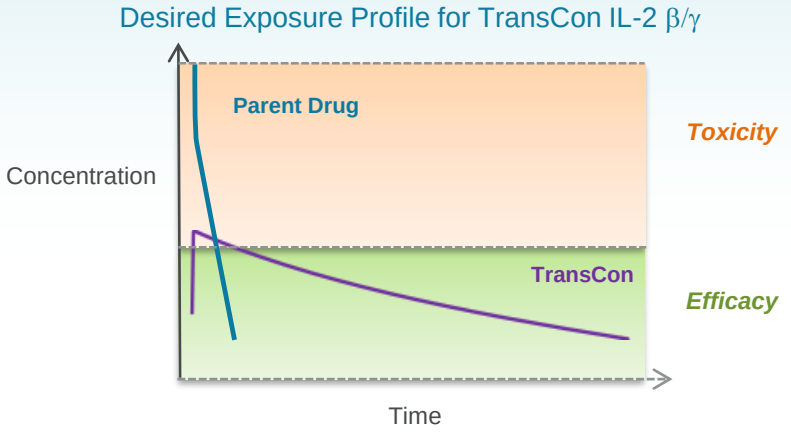
IL-2Rα/β/γ activation:
Promotes Tregs
Promotes Eosinophils

Limit anti-tumor responses, mechanism of AEs

IL-2Rβ/γ activation
Promotes CD8⁺ T cells
Promotes NK cells

Promote anti-tumor responses

2) Generate a product with long-lasting exposure avoiding high Cmax



Onur B, et al. *Biomed Intell*. 2019; 149:w14697.

Design of TransCon IL-2 β/γ: 1) Designed for Desired Receptor Binding

Generation of IL-2 Variant

Introduction of cysteine at α–binding site of IL-2 (aldesleukin)

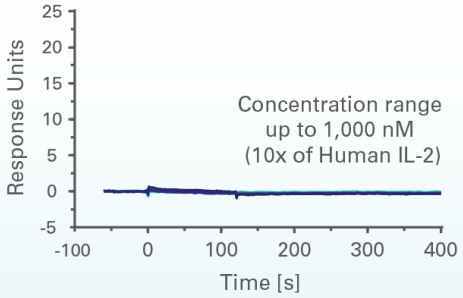
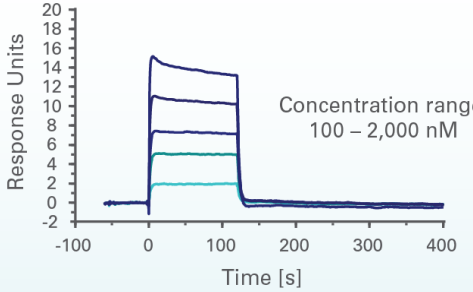
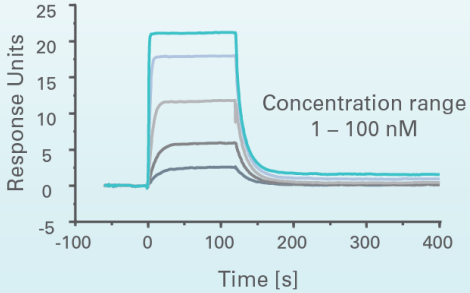
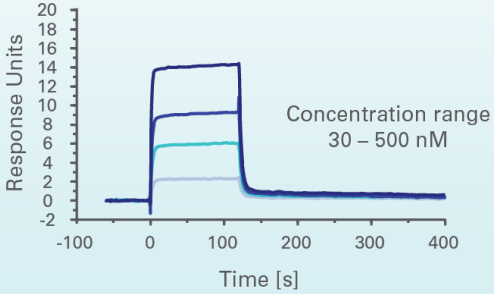
Blocking IL-2Rα–binding

Site-selective permanent PEG conjugation (5kDa) of introduced cysteine

IL-2 (gold) with IL-2 alpha-receptor (grey)

Optimized IL-2 β/γ receptor selectivity and potency by permanent site-selective PEG conjugation at IL-2Rα–binding site

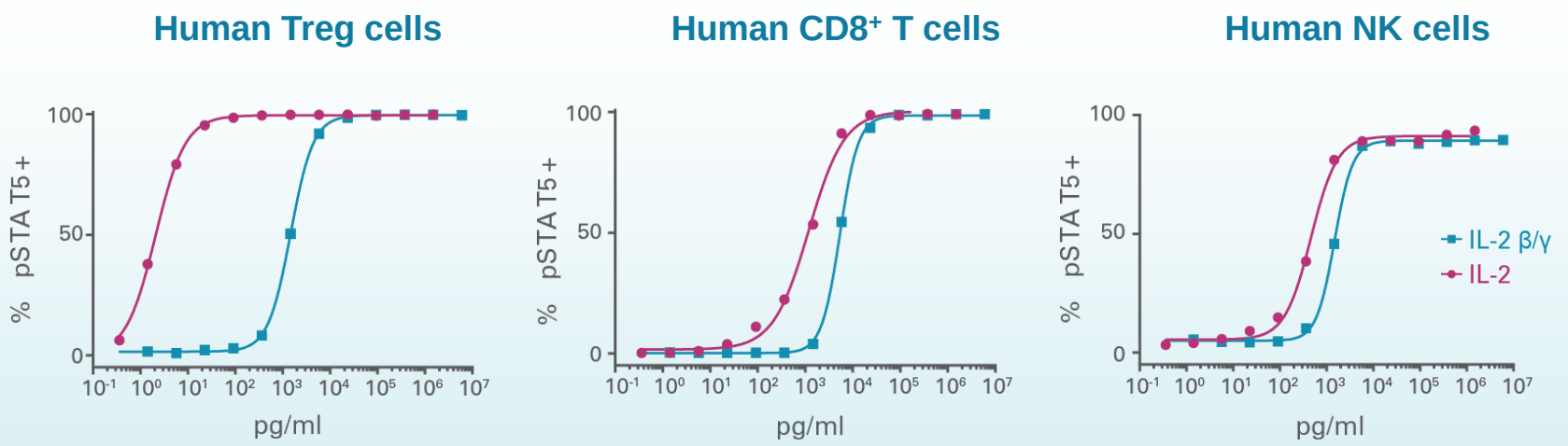
Receptor Selectivity Demonstrated in Binding Assays

	Binding to IL-2R α-chain	Binding to IL-2R β-chain
IL-2 β/γ		
Human IL-2		

IL-2 β/γ demonstrated strong receptor bias with reduced IL-2Rα binding and well-retained IL-2Rβ binding

Rosen D, et al. AACR annual meeting. 2020; Poster 4507.

Receptor Selectivity Confirmed in Primary Human Cells

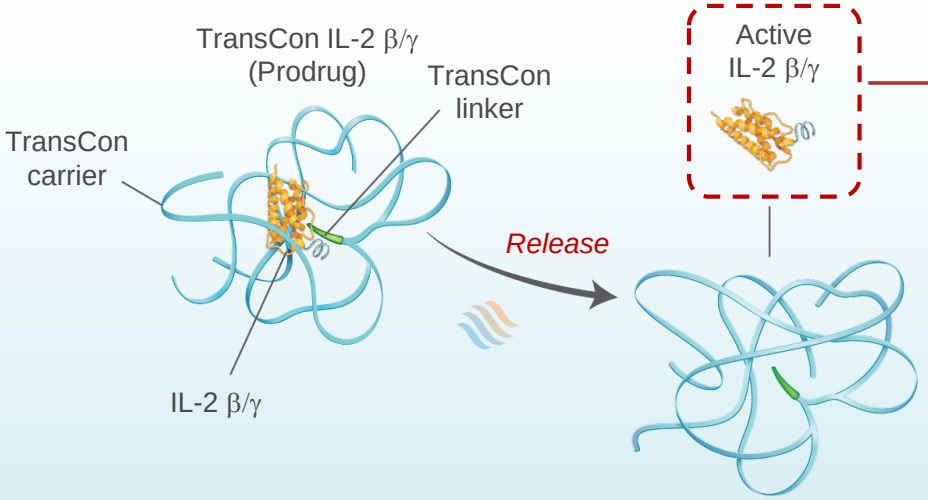


Substantially reduced potency on primary human Treg cells compared to rhIL-2 with minimal potency loss on CD8+ T cells and NK cells

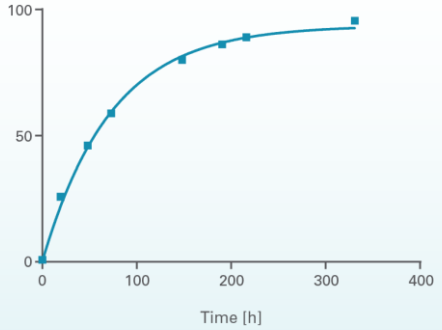
Rosen D, et al. AACR annual meeting. 2020; Poster 4507.

Design of TransCon IL-2 β/γ: 2) TransCon Technology to Optimize Exposure

TransCon linker slowly releases IL-2 β/γ



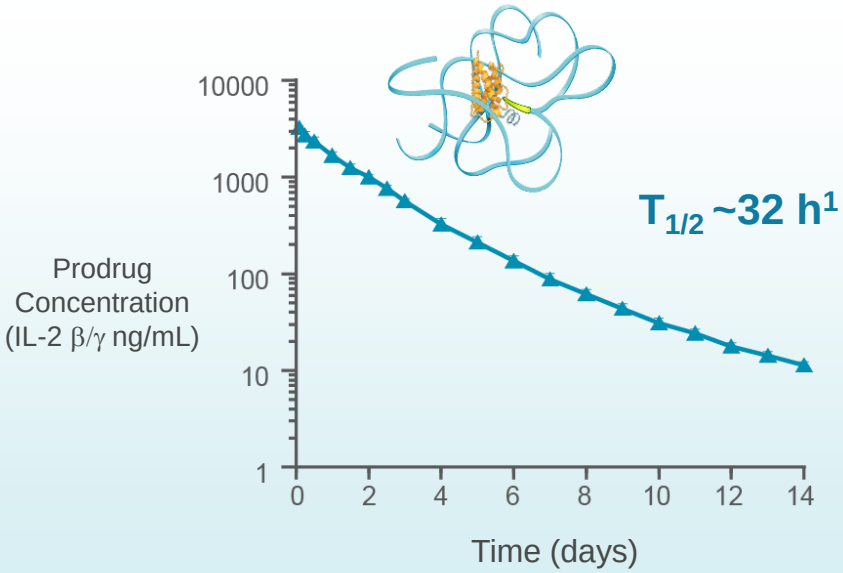
TransCon IL-2 β/γ *in vitro* release kinetics



Sustained, long-lasting exposure utilizing the TransCon hGH linker and carrier, potential to support every 3-week dosing

Rosen D, et al. AACR annual meeting. 2020; Poster 4507.

TransCon IL-2 β/γ Resulted in Long-lasting Exposure in NHP



- TransCon IL-2 β/γ plasma PK in NHP demonstrated prolonged, sustained release of IL-2 β/γ
- $T_{1/2}$ of TransCon IL-2 β/γ prodrug and released IL-2 β/γ[2] was ~32 h

PK profile supports potential best-in-class properties

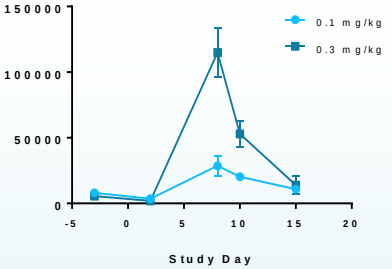
NHP = non-human primates.
[1]Rosen D, et al. AACR annual meeting. 2020; Poster 4507.
[2]Data on file.

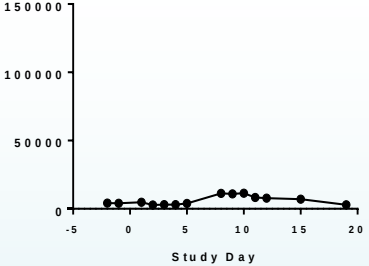
Robust Increase in Lymphocyte Count with Minimal Eosinophil Expansion in NHP

TransCon IL-2 β/γ[1] (Single Dose on Day 1)

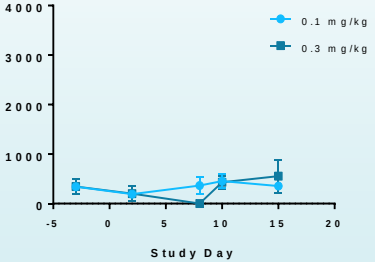
Aldesleukin[2] (0.4 mg/day on Days 1-5)

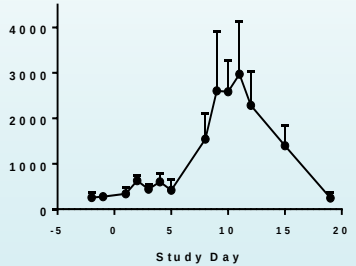
Absolute Lymphocyte Count / µL





Eosinophil Count / µL





Doses are indicated as mg/kg; average animal weight 3.13 kg (2.46 – 3.69 kg)

Doses are indicated as mg/animal; average animal weight 9.2 kg (7.7 – 10.6 kg)

Single dose provided >10-fold and prolonged enhancement of lymphocyte counts supporting Q3W dosing; minimal effect on eosinophils suggests low risk of vascular leak syndrome syndrome[3,4]

Q3W = every 3 weeks

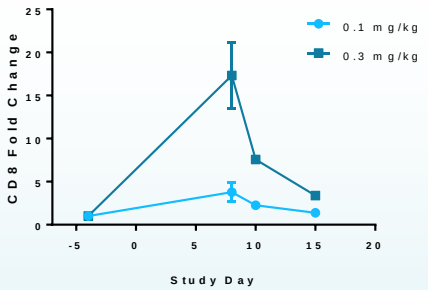
[1]Data on file. [2]Rosen D, et al. AACR annual meeting. 2020; Poster 4507.
[3]Rand, et al. *J Clin Invest*. 1991; 88: 825. [4]Van Haelst Pisani C, et al. *Blood.* 1991;78:1538.

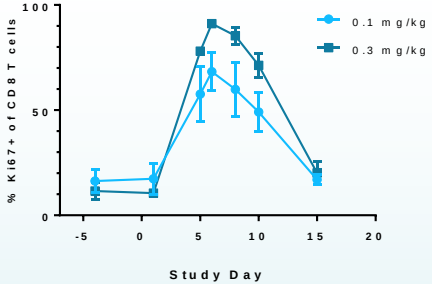
Potent CD8+ T Cell and NK Cell Expansion and Activation in NHP

Fold Change*

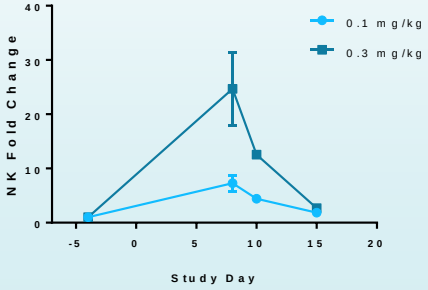
% Ki67+

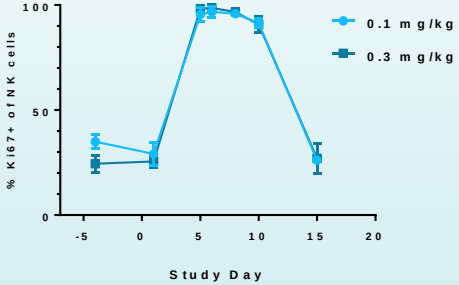
CD8+ T cells





NK cells



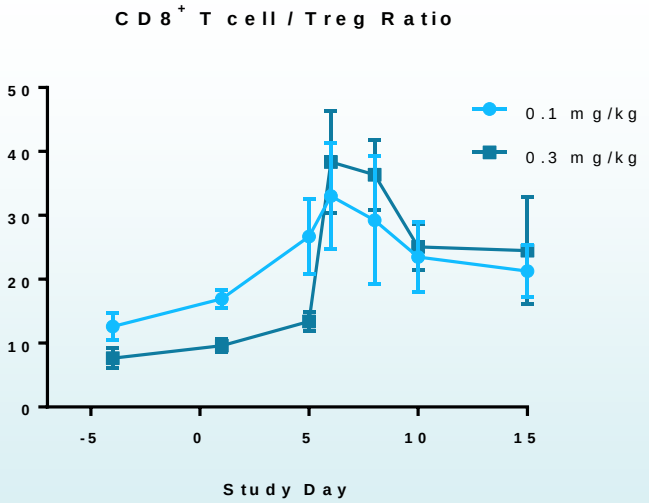


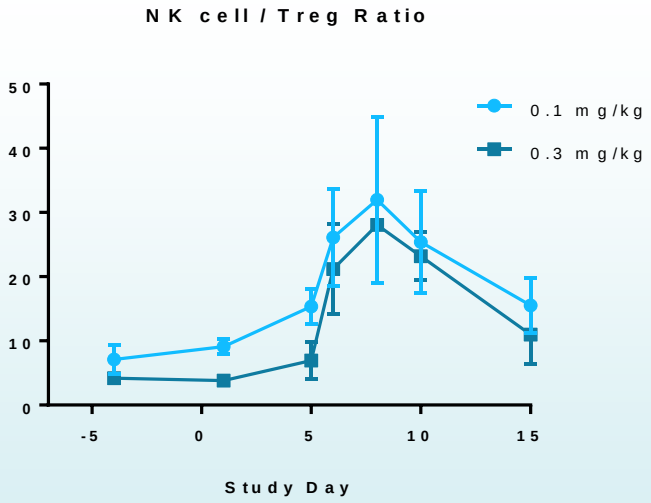
Expansion and activation of cytotoxic lymphocyte subsets observed following a single dose of TransCon IL-2 β/γ

*Fold change using cell counts derived from hematology lymphocyte counts and flow cytometry-based frequencies within lymphocytes.
Data on file.

TransCon IL-2 β/γ Expands Ratios of CD8+ T Cells and NK Cells Over Treg Cells in NHP

Cell ratios following a single dose of TransCon IL-2 β/γ on Day 1

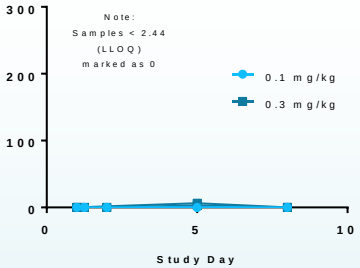
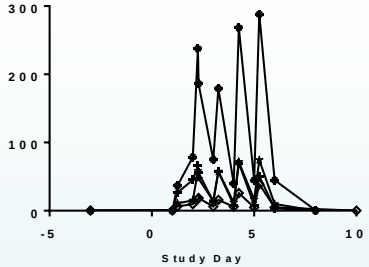
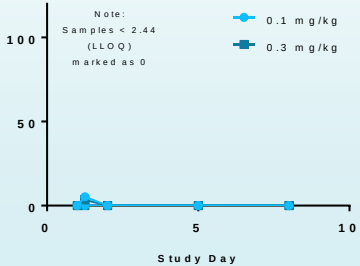
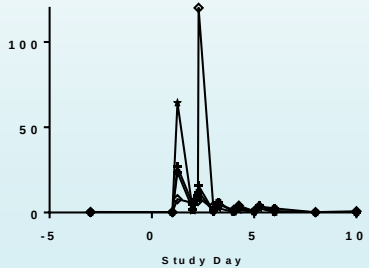




Consistent with observed minimal binding to IL-2Rα, the ratios of CD8+ T cells and NK cells over Treg cells increased following administration of TransCon IL-2 β/γ in NHP

Data on file.

Single Dose TransCon IL-2 β/γ Induced Lower Levels of Systemic Inflammation Markers in NHP When Compared to Aldesleukin

	TransCon IL-2 β/γ[1] (Single dose)	Aldesleukin[2] (0.4 mg/day x 5)	
IL-5 (pg/ml)			Minimal IL-5 predicts minimal eosinophil induction
IL-6 (pg/ml)			Minimal IL-6 predicts low risk of cytokine-release syndrome
	Doses are indicated as mg/kg; average animal weight 3.13 kg (2.46 – 3.69 kg)	Dose is indicated as mg/animal; average animal weight 9.2 kg (7.7 – 10.6 kg)	

TransCon IL-2 β/γ IND or similar expected in Q3 2021

[1]Data on file.
[2]Rosen D, et al. AACR annual meeting. 2020; Poster 4507.

Evaluation of Immune Memory and Potential Cross-immunity Following TransCon IL-2 β/γ plus TransCon TLR7/8 Agonist

Syngeneic CT26 tumor model (colon-derived tumor line)

Treatment with TransCon IL-2 β/γ + TransCon TLR7/8 Agonist

Re-challenge of complete responders with CT26

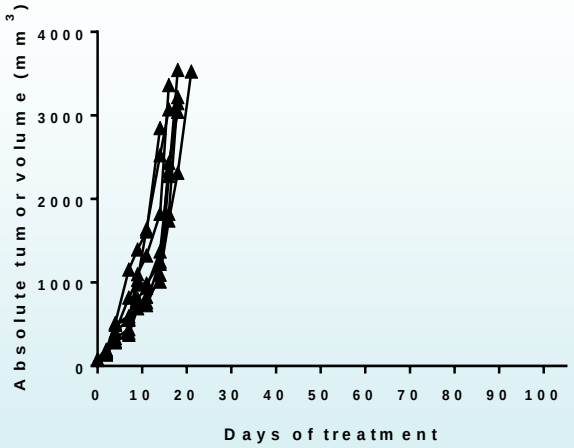
- 73 days after initial treatment
- No new treatment

Challenge of complete responders with different tumor type, EMT6 (mammary-derived)

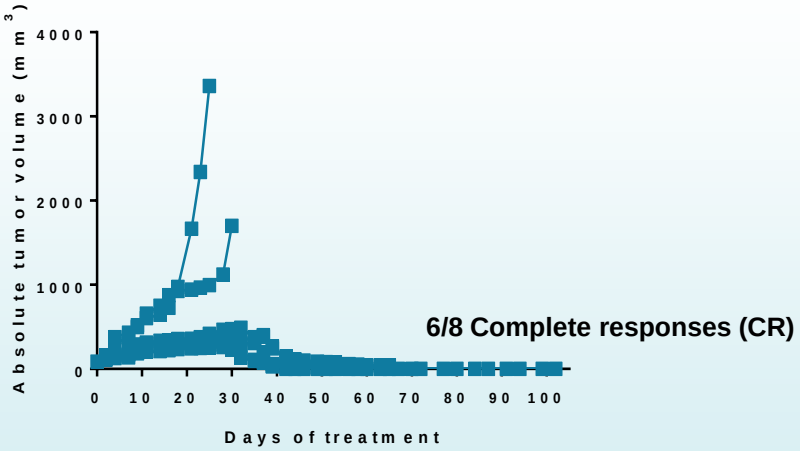
- 28 days after CT26 re-challenge
- No new treatment

TransCon IL-2 β/γ Plus TransCon TLR7/8 Agonist Resulted in Durable Complete Tumor Regressions in the CT26 Tumor Model

Buffer control



TransCon IL-2 β/γ (3 doses) + TransCon TLR7/8 Agonist (single dose)

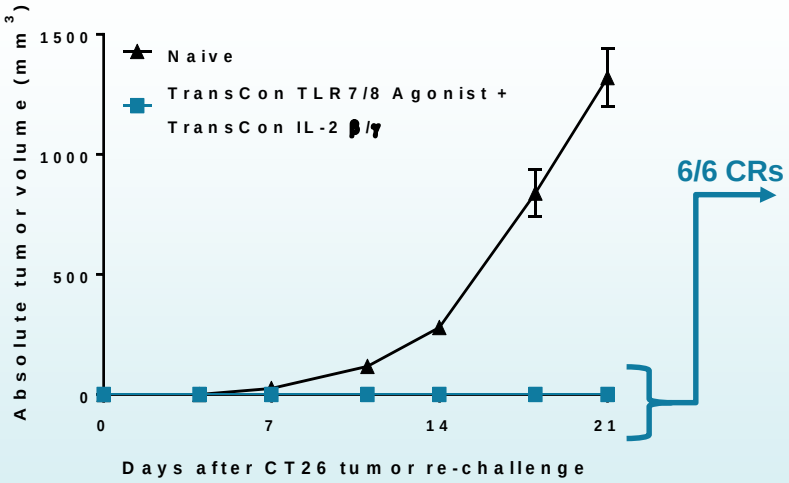


The immune activating mechanism of action of TransCon IL-2 β/γ plus TransCon TLR7/8 Agonist and complete responses suggests potential for anti-tumor immune memory

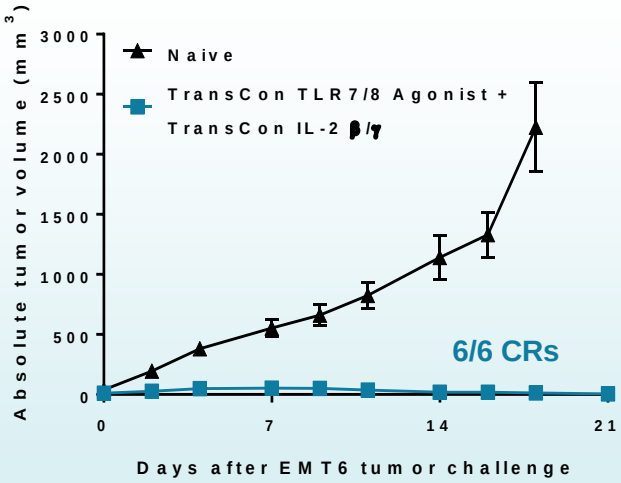
Data on file.

Potent Immune Memory and Cross-reactive Anti-tumor Response Against a New Tumor Type

CT26 re-challenge of CRs (colon-derived tumor line)



EMT6 challenge of CRs (mammary-derived tumor line)



Protection against initial tumor and a new tumor type, suggesting potent anti-tumor memory and cross-reactive anti-tumor immunity

Data on file.

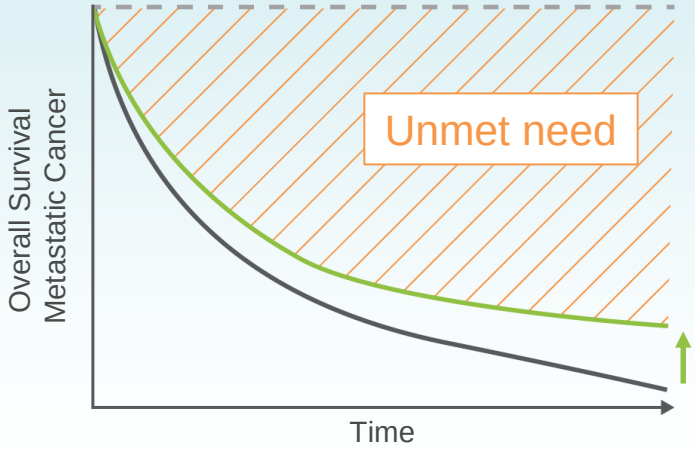
Potential Paradigm Shift to How Cancer is Treated

- TransCon technologies may enable a new treatment paradigm building upon well-known biology
- Two near-term IND candidates demonstrating potentially best-in-class properties
  - TransCon TLR7/8 Agonist designed for intratumoral, long-term sustained release for superior efficacy with minimal systemic adverse events
  - TransCon IL-2 β/γ designed for IL-2Rβ/γ selectivity, combined with low Cmax and long exposure
  - Combination resulted in potent anti-tumor responses and immunological memory, including cross-immunity against a new tumor type
- TransCon TLR7/8 Agonist IND planned by year-end 2020; TransCon IL-2 β/γ IND or similar planned for Q3 2021

Clinical Strategy

Unmet Medical Need Remains High Despite Advancements

- Immunotherapy has given hope for dramatic improvement in cancer treatment…
- But most cancer patients today are not benefiting from immunotherapy



- U.S. cancer patients eligible for checkpoint inhibitors (CPI) increased from 1.5% in 2011 to 43.6% in 2018
- Percentage of patients estimated to respond to CPI was 0.1% in 2011 and increased to 12.5% in 2018

Immunotherapy has "raised the tail" for multiple tumor types

More effective therapies are urgently needed

Haslam A and Prasad V. *JAMA Netw Open*. 2019;2(5):e192535.

ascendis pharma

Clinical Development Strategy in Oncology to Take Advantage of the Clinically Validated TransCon Platform

BUILD

safety and tolerability profile while identifying appropriate dose

- Across various indications
- As monotherapy and in combination with standard of care
- In combination with internal pipeline

ESTABLISH

proof-of-concept efficacy in indications of high unmet medical need

- Indications with strong scientific rationale
- Available benchmark data

EXPAND

to other indications based on

- Unmet need
- Emerging data and changing treatment landscape

Phase 1/2 Dose Escalation and Dose Expansion Study of TransCon TLR7/8 Agonist Alone or in Combination with CPI

Dose Escalation ("3+3" Design) | Dose Expansion

Part 1: Monotherapy

Any solid tumor, any line

Part 2: Combination with CPI

Indications with known CPI activity

Part 3: Combination with CPI

Multiple indication-specific cohorts at Recommended Ph2 Dose (RP2D)

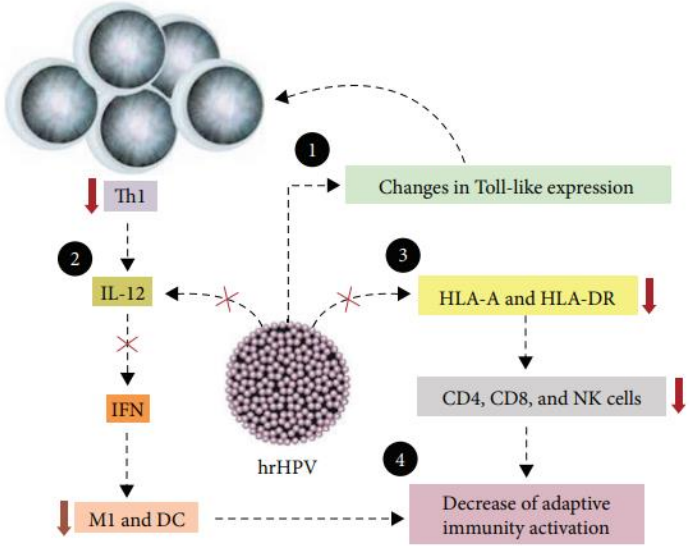
Objectives:

- Safety and tolerability; define MTD and RP2D
- Pharmacokinetics / pharmacodynamics (PK/PD)
- Preliminary anti-tumor efficacy (ORR, duration of and time to response)

MTD: maximum tolerated dose; ORR: overall response rate using RECIST 1.1

Initial Indication Selection Based on Strong Scientific Rationale to Focus on HPV-associated Cancers

TLRs and HPV-associated cancers[1]



Dose Expansion

Combination with CPI

HPV-associated tumors:

- HNSCC
- Others (anal, cervical, vulvar, penile, vaginal)

Other indications will be added based on

- Unmet need
- Emerging data and changing treatment landscape

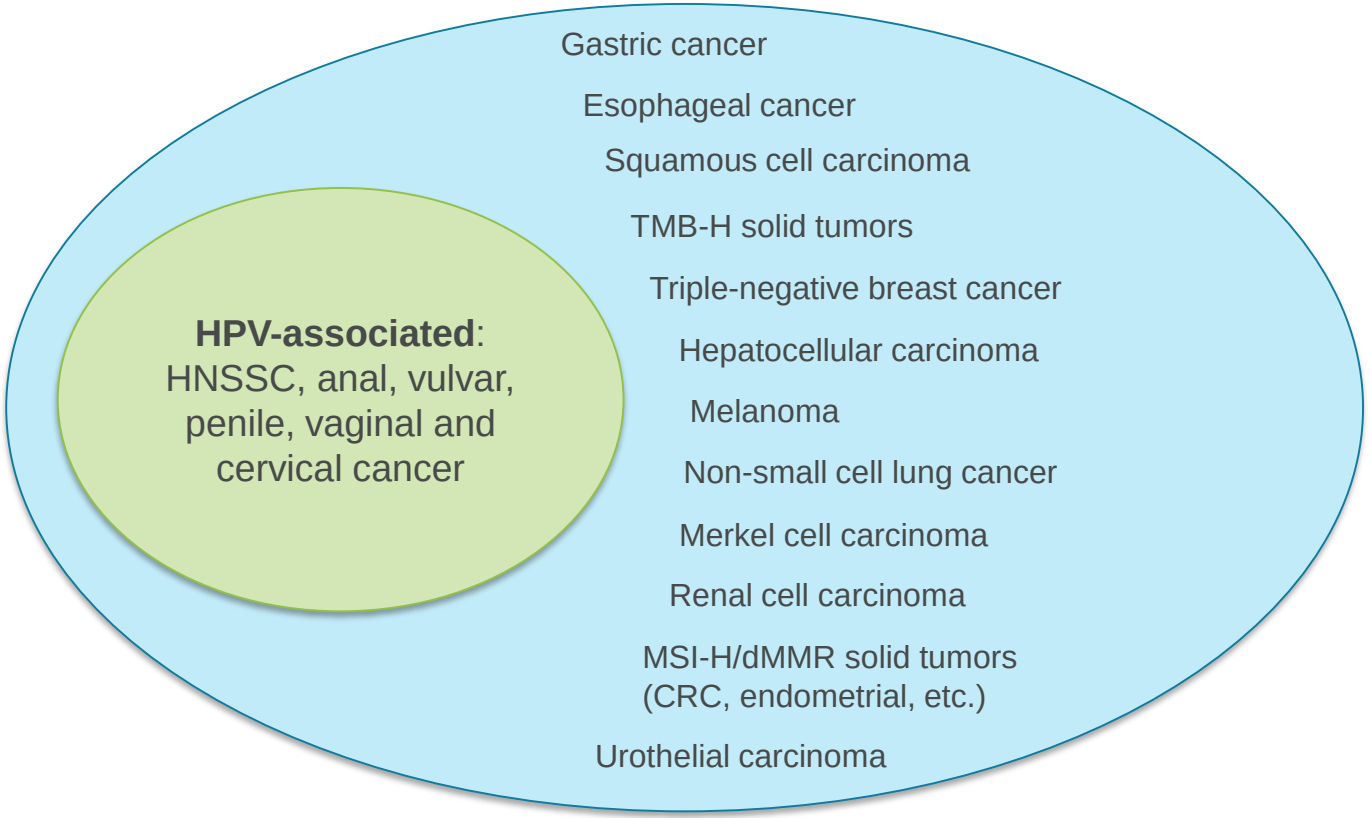
HNSCC: HPV+ prevalence rising -- for every 2 new cases of HPV-oropharyngeal carcinoma diagnosed, 5 new cases HPV+[2]

Anal, cervical, vulvar, penile, vaginal: vast majority (>70-90%) are HPV+

HNSCC: head and neck squamous cell carcinoma;
HPV: human papillomavirus

[1]Barros M, et al. *J Immunology Res.* 2018; 2912671:1-17.
[2]Mahal B, et al. *Cancer Epidemiol Biomarkers Prev*. 2019; 10:1660-1667.

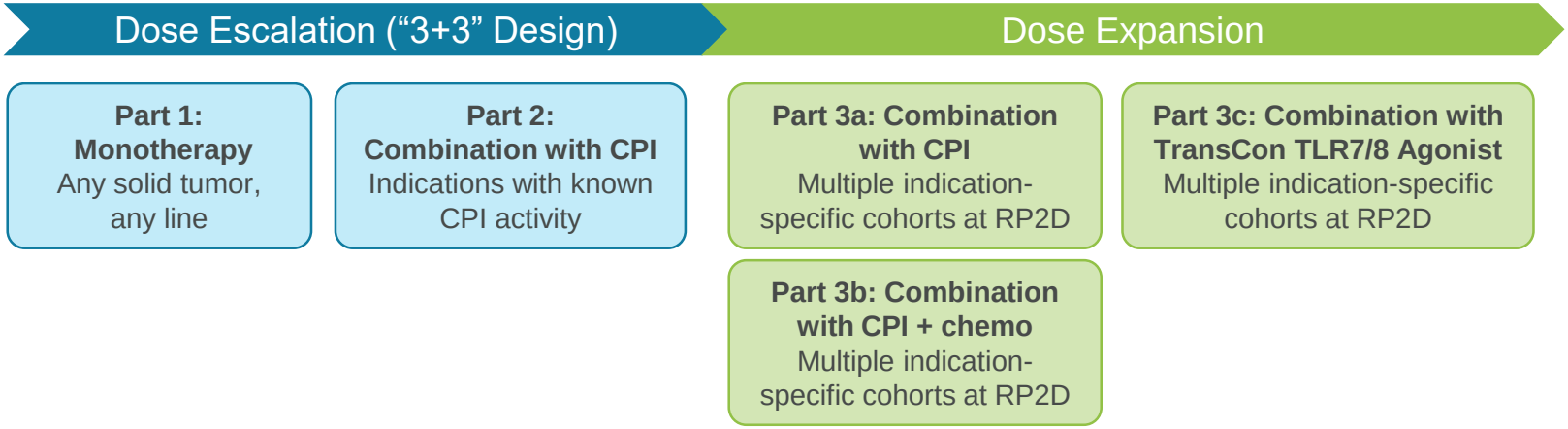
TransCon TLR7/8 Agonist: Potential to Expand to Other Indications



TransCon TLR7/8 Agonist - Summary

- Sustained IT delivery using the validated TransCon platform offers a new treatment paradigm with potential for superior efficacy and safety
- IND submission anticipated by year-end 2020
  - Engaging major academic centers
- Clinical development strategy aims to:
  - Build safety and tolerability profile across multiple indications and with standard of care combination partner
  - Establish proof-of-concept efficacy, focusing on indications of high unmet need that have strong scientific rationale for TLR7/8 agonists
  - Expand to other indications based on unmet need and changing treatment landscape

Phase 1/2 Dose Escalation and Expansion Study of TransCon IL-2 β/γ Alone or in Combination with CPI and TransCon TLR7/8 Agonist



Objectives:

- Safety and tolerability; define MTD and RP2D
- Pharmacokinetics / pharmacodynamics (PK/PD)
- Preliminary anti-tumor efficacy (ORR, duration of and time to response)

TransCon IL-2 β/γ – Potential Backbone Agent in Oncology

- TransCon IL-2 β/γ has potential to be the best-in-class IL-2 molecule
- IND or similar submission anticipated in Q3 2021
- Clinical development strategy aims to:
  - Build safety and tolerability profile across multiple indications and with standard of care combination partners and internal pipeline
  - Establish proof-of-concept efficacy, focusing on indications of high unmet need that derive insufficient benefit from checkpoint inhibitors alone
  - Expand to other indications based on unmet need and changing treatment landscape

Oncology Summary

- Best-in-class potential using systemic and intratumoral TransCon technologies
- Differentiated product candidates
  - TransCon TLR7/8 Agonist
    - Potential to improve efficacy and practicality of intratumoral treatments
    - IND expected for TransCon TLR7/8 Agonist by year-end 2020
  - TransCon IL-2 β/γ
    - Potential to become a backbone agent in oncology
    - IND or similar expected TransCon IL-2 β/γ in Q3 2021
- Opportunity to expand pipeline to impact all aspects of anti-tumor response
  - Large number of validated oncology targets with known limitations

Aiming to help cancer patients live longer and better!

Q&A Session