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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

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**FORM 6-K**

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**REPORT OF FOREIGN PRIVATE ISSUER  
PURSUANT TO SECTION 13a-16 OR 15d-16  
UNDER THE SECURITIES EXCHANGE ACT OF 1934**

For the month of November, 2020

Commission File Number: 001-36815

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**Ascendis Pharma A/S**

(Exact Name of Registrant as Specified in Its Charter)

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Tuborg Boulevard 12  
DK-2900 Hellerup  
Denmark  
(Address of principal executive offices)

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Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F       Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

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Spokespersons of Ascendis Pharma A/S (the “Company”) presented the information in the presentation slides attached hereto as Exhibit 99.1 in a webcast on November 20, 2020.

The furnishing of the attached presentation is not an admission as to the materiality of any information therein. The information contained in the presentation is summary information that is intended to be considered in the context of more complete information included in the Company’s filings with the Securities and Exchange Commission (the “SEC”) and other public announcements that the Company has made and may make from time to time. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing or furnishing of other reports or documents with the SEC or through other public disclosures.

**Exhibits**

99.1 [Company Presentation](#)

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Ascendis Pharma A/S**

Date: November 20, 2020

By: /s/ Michael Wolff Jensen

Michael Wolff Jensen

Chairman and Senior Vice President, Chief Legal Officer



# 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.

Oncology product rights owned by Ascendis Pharma Oncology Division A/S (a wholly owned subsidiary of Ascendis Pharma A/S).  
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# 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 $\beta/\gamma$

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<sup>1</sup> 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  $\beta/\gamma$  IND filing or similar expected in Q3 2021
- As of September 30, 2020, cash, cash equivalents and marketable securities of €957.5 million



# 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

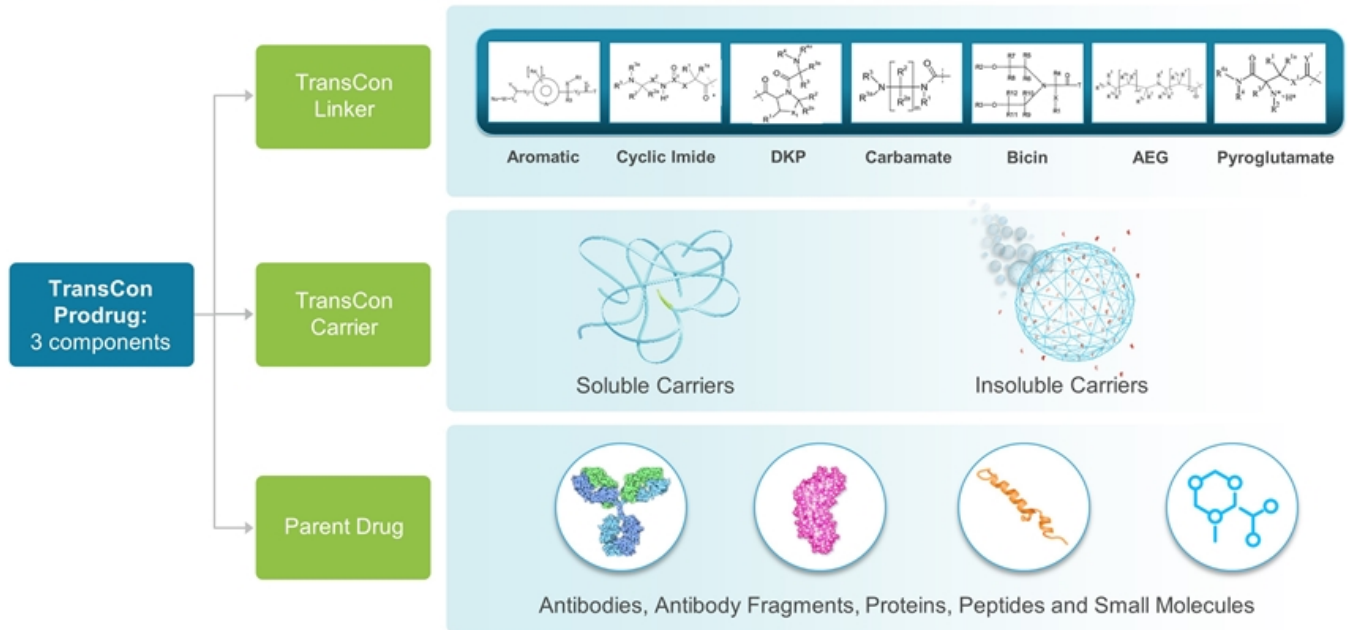
Conventional technologies (protein enlargement and encapsulation) are associated with altered biology and unpredictable drug release

## The Revolutionary Solution

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

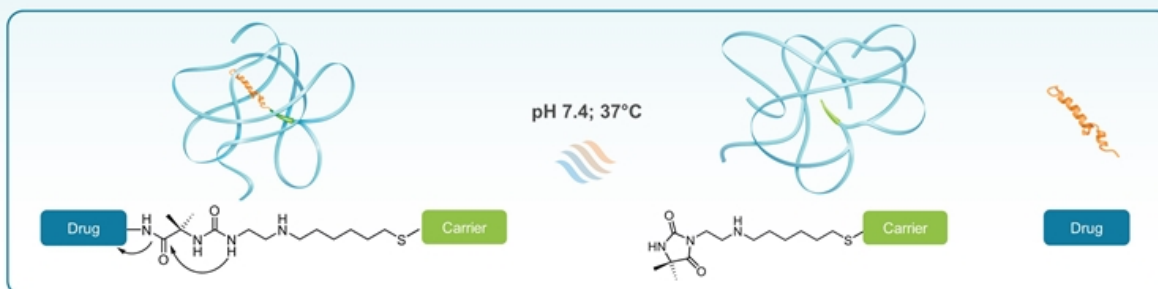
TransCon technology reversibly conjugates a drug to a carrier and predictably releases the unmodified drug under physiological conditions

# Transient Conjugation: A Powerful, Flexible Platform

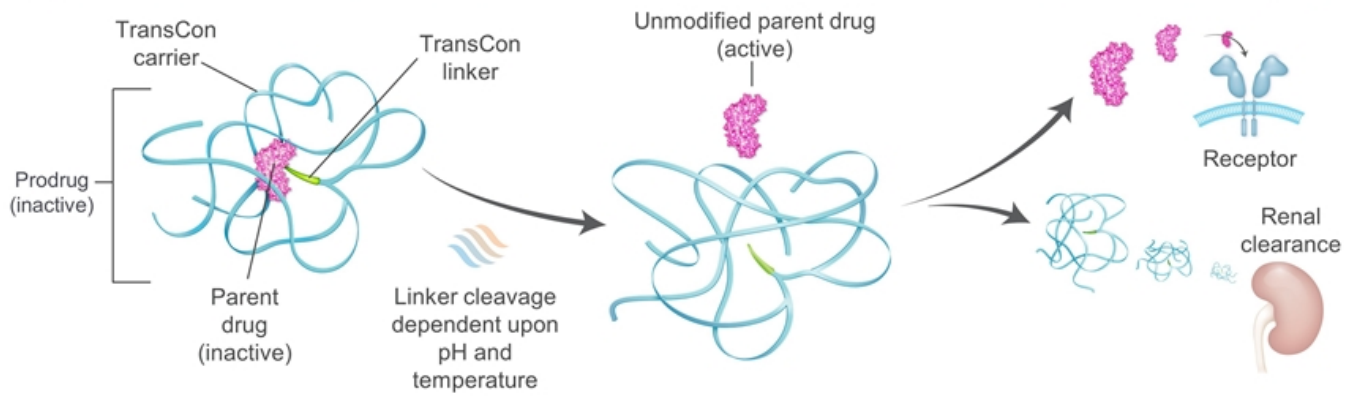


## TransCon Technology: The TransCon Linker

- 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

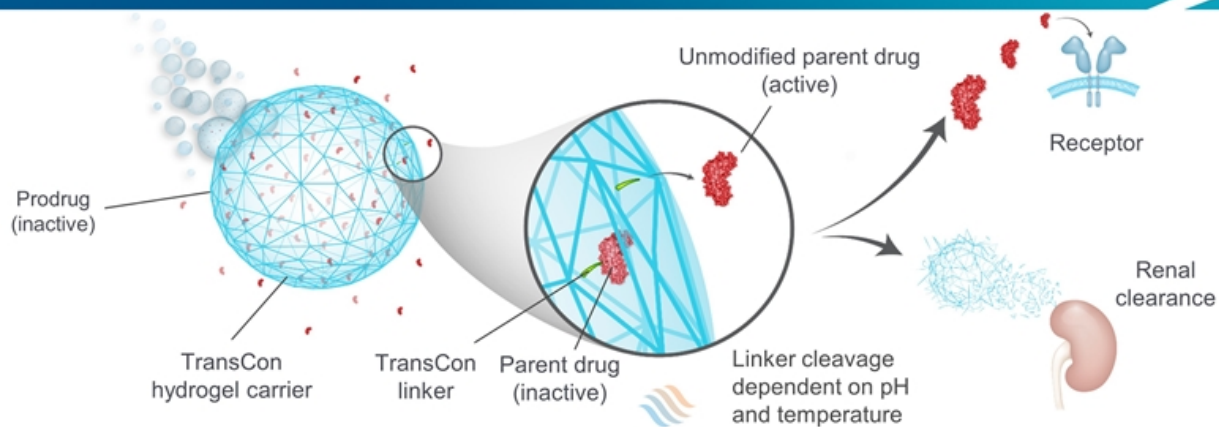


Parent drug is transiently bound to a TransCon linker-soluble carrier moiety, which inactivates and shields parent drug from clearance

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



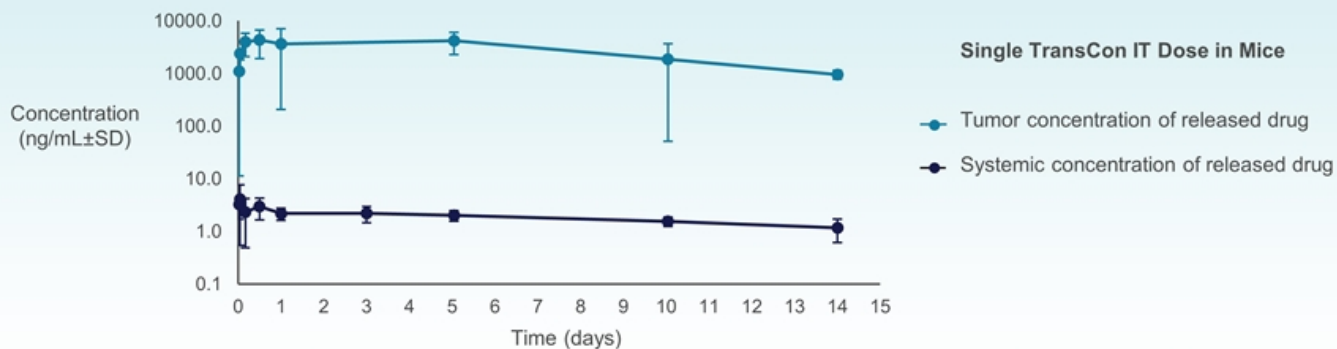
Parent drug is transiently bound to TransCon linker-hydrogel carrier, which inactivates, shields parent drug and prevents clearance

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



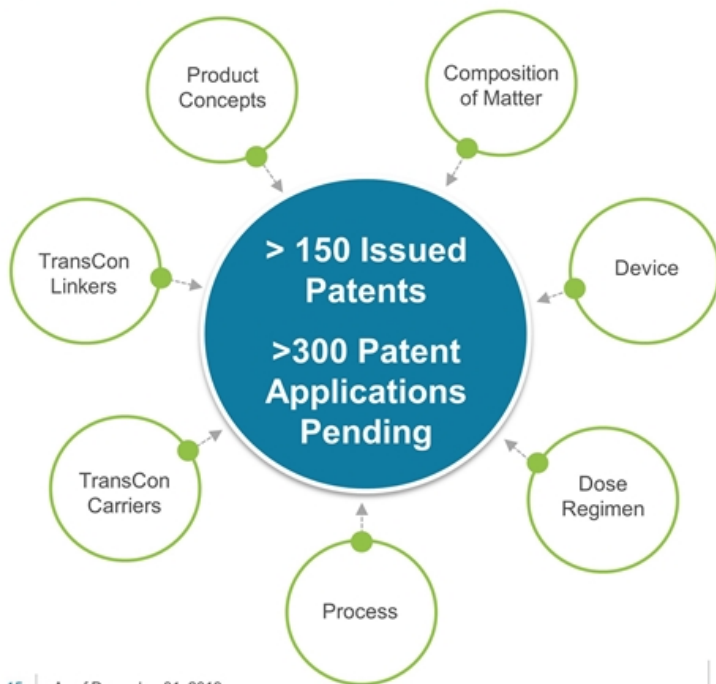
# Algorithm Used in Endocrinology Used to Build Oncology Pipeline



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 3<sup>rd</sup> 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

## 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

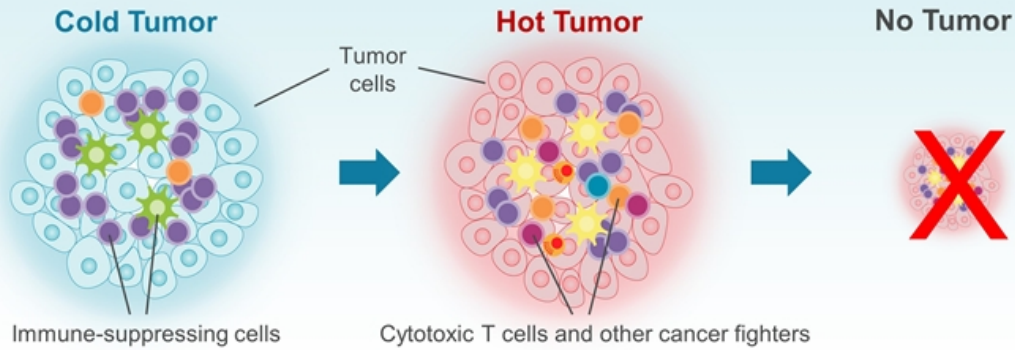
**Juha Punnonen, M.D., Ph.D.**  
*SVP, Head of Oncology*

**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

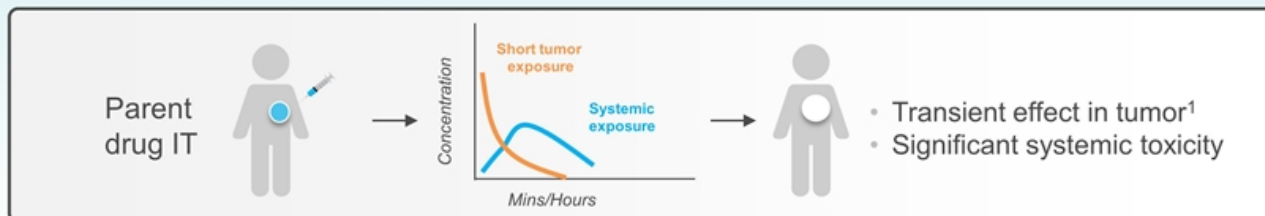


Applicable for diverse drug classes and mechanisms of action; opportunity for combination approaches

- 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<sup>1</sup>, high systemic Cmax and need for frequent dosing



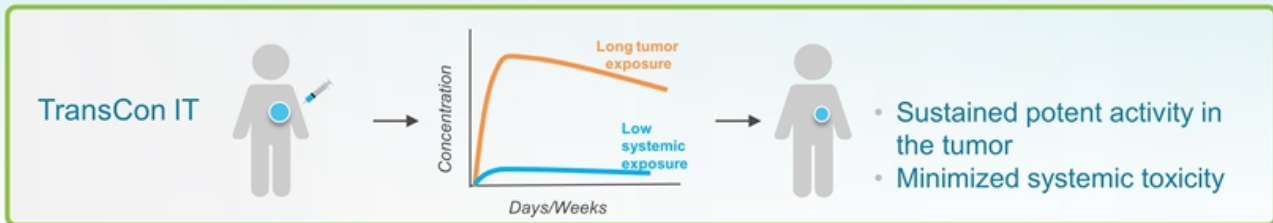
TransCon technology has the potential to overcome the limitations of conventional intratumoral treatments

20 | <sup>1</sup> 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.

All product candidates are investigational. For investor communication only. Not for use in promotion or product commercialisation.

# TransCon IT Aims to Transform Intratumoral Treatments

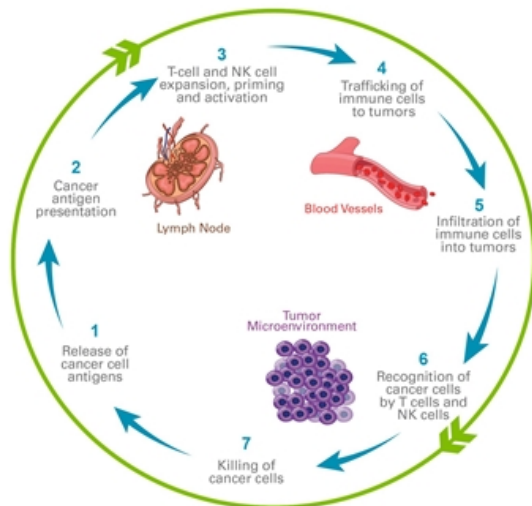
- Slow IT release allows for potential activity in tumor and draining lymph nodes for weeks or months, while keeping systemic exposure minimal
- Designed to enable new multi-agent combinations without added toxicity
- Potential for long dosing interval enabling treatments of hard-to-access tumors



TransCon 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 $\beta/\gamma$

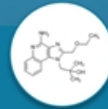
Designed to aid T cell and NK cell expansion, priming and activation as well as infiltration of immune cells in tumors (steps 3 and 5).

## 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

## 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

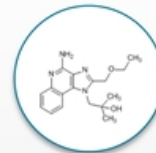
## Safety

- 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

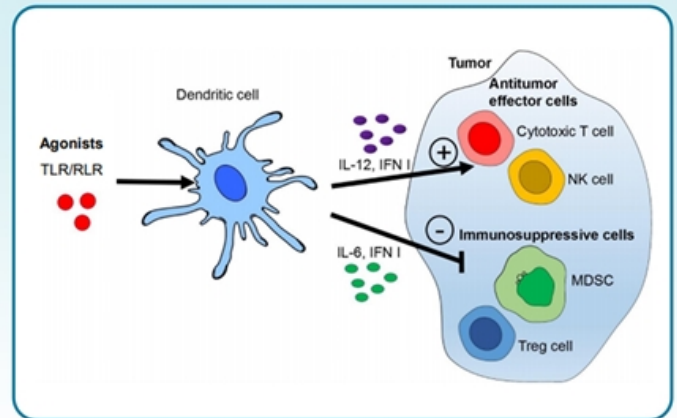


Designed for intratumoral, sustained release with **minimal systemic exposure** aiming for **superior efficacy**

# 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

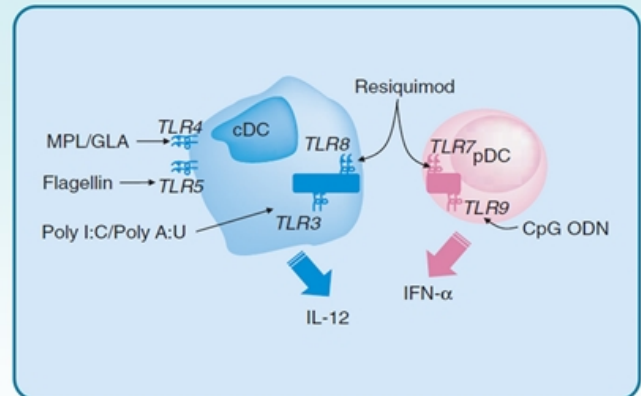
# Resiquimod: TLR7/8 Agonist<sup>1,2</sup>

- 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- $\alpha$ , IL-1, chemokines
- Enhances antigen presentation: upregulated MHCII, costimulatory molecules (e.g. CD80/86)
- Enhances anti-tumor immunity

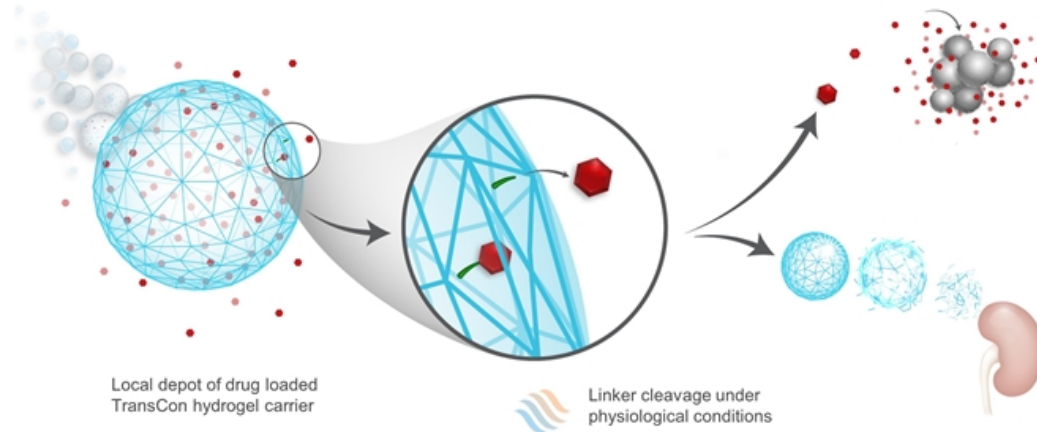


## Resiquimod activates both conventional DCs and pDCs

26 | <sup>1</sup> Vasilakos J and Tomai M. *Exp Rev Vaccines*, 2013; 12:809-819.  
<sup>2</sup> Rook A, et al. *Blood*. 2015;126(25):2765.

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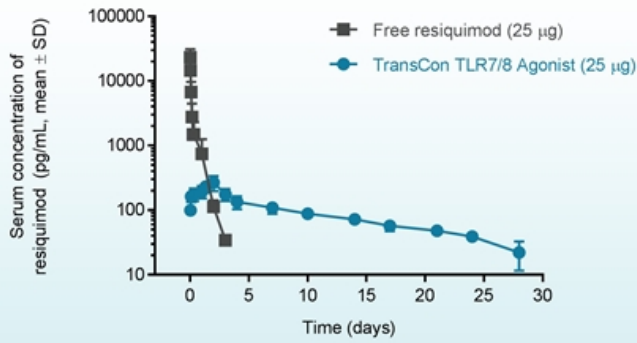
# TransCon TLR7/8 Agonist: Sustained Intratumoral Release of Resiquimod



- 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

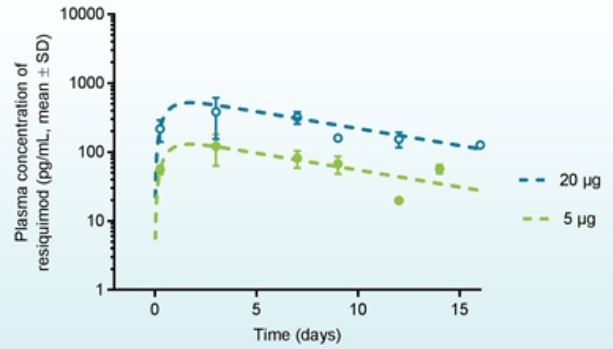
# TransCon TLR7/8 Agonist Resulted in Sustained Release of Resiquimod over Several Weeks

Subcutaneous administration in rats



Parent Drug (free resiquimod):  $T_{1/2} = \sim 10$  h  
TransCon TLR7/8 Agonist:  $T_{1/2} \sim 10$  days

Intratumoral (CT26) administration in mice

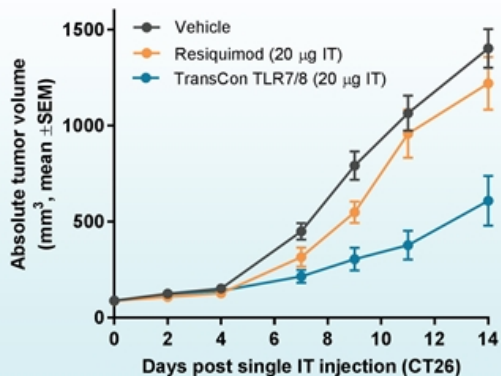


TransCon TLR7/8 Agonist:  $T_{1/2} \sim 12$  days

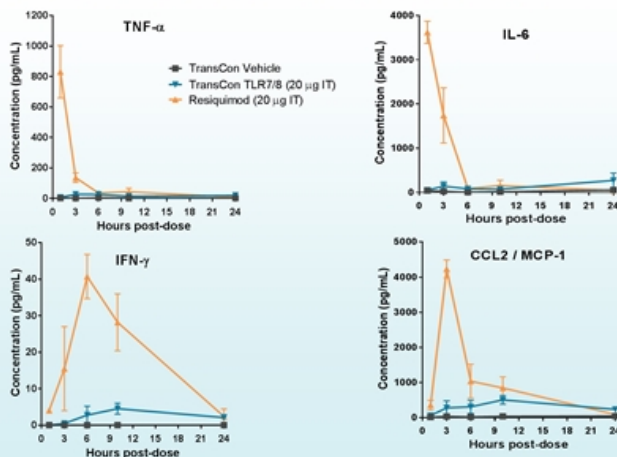
TransCon technology enables 25-fold increased half-life and avoids high Cmax

# 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

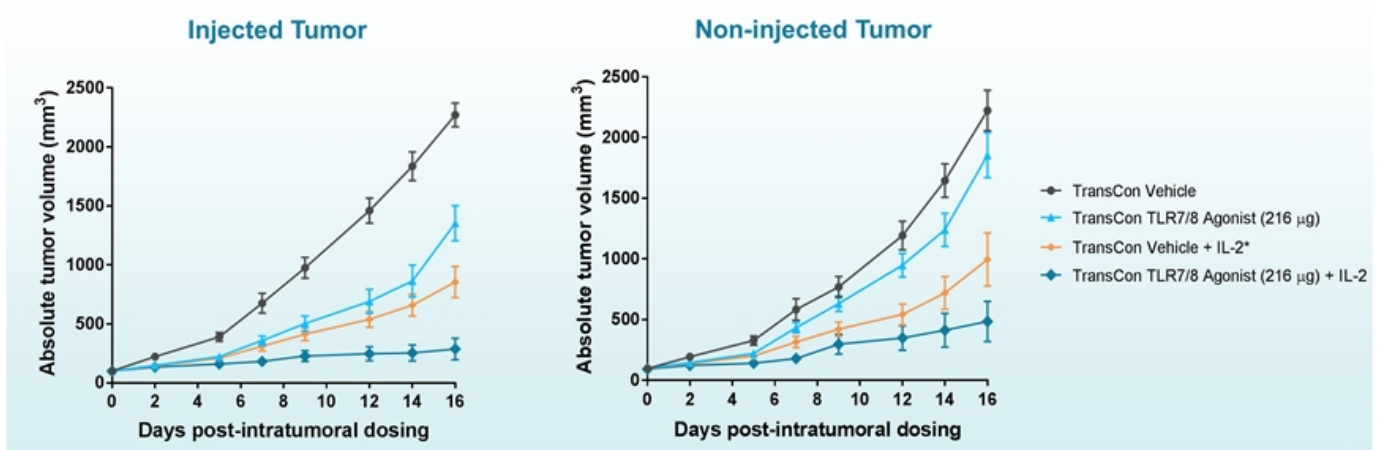


TransCon TLR7/8 Agonist has the potential to provide more potent anti-tumor benefits without dose-limiting toxicity, as IL-6 and TNF- $\alpha$  associate with cytokine release syndrome in patients<sup>1,2</sup>



# 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)



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

30 | \*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.

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# Product Candidates in Oncology

*IL-2 Selective for the IL-2R $\beta/\gamma$*



TransCon  
IL-2  $\beta/\gamma$

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

## Suboptimal receptor binding

- Two receptors: IL-2R $\alpha/\beta/\gamma$  and IL-2R $\beta/\gamma$
- $\alpha/\beta/\gamma$  receptor activates Tregs and endothelial cells, reducing efficacy and increasing risk of capillary leak syndrome

## Suboptimal PK

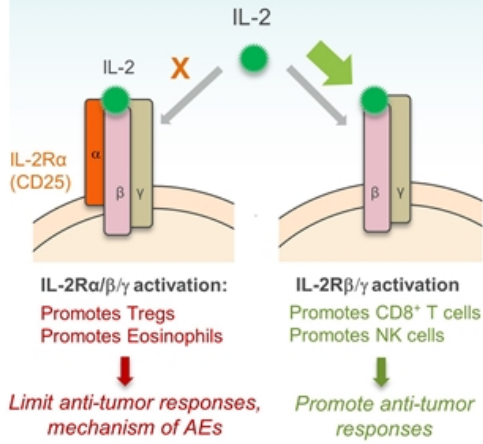
- Short half life of IL-2 (~1.5 h)
- High Cmax and pulsatile dosing drive adverse events

- 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

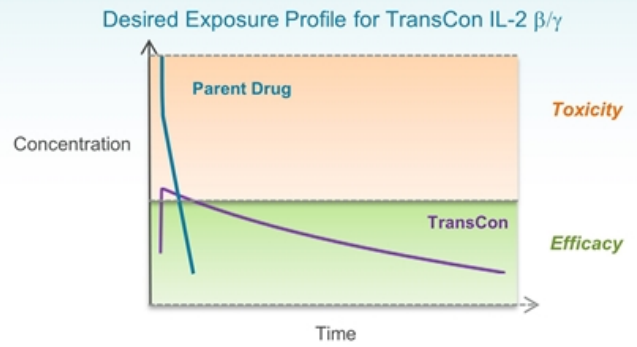
1)

Prevent IL-2R $\alpha$  binding to selectively activate IL-2R $\beta/\gamma$



2)

Generate a product with long-lasting exposure avoiding high C<sub>max</sub>

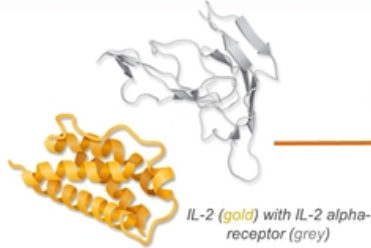


# Design of TransCon IL-2 $\beta/\gamma$ :

## 1) Designed for Desired Receptor Binding

### Generation of IL-2 Variant

Introduction of cysteine at  $\alpha$ -binding site of IL-2 (aldesleukin)



### Blocking IL-2R $\alpha$ -binding

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

Permanent PEG attachment at  $\alpha$ -binding site

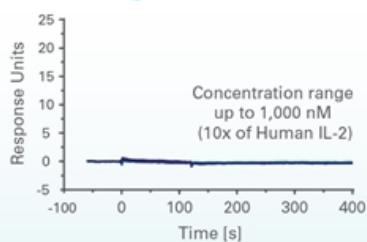


Optimized IL-2  $\beta/\gamma$  receptor selectivity and potency by permanent site-selective PEG conjugation at IL-2R $\alpha$ -binding site

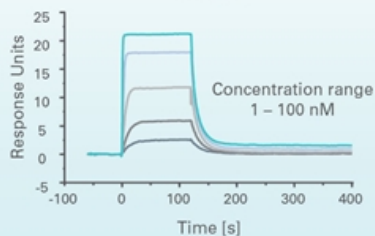
# Receptor Selectivity Demonstrated in Binding Assays

## Binding to IL-2R $\alpha$ -chain

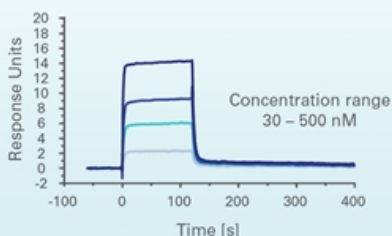
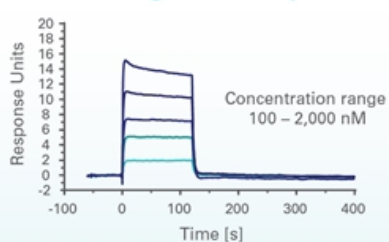
IL-2  $\beta/\gamma$



Human IL-2



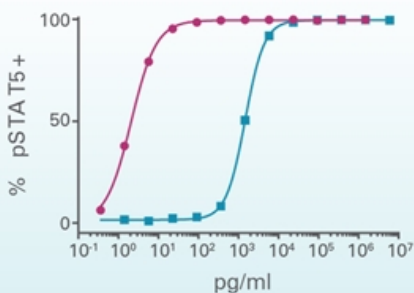
## Binding to IL-2R $\beta$ -chain



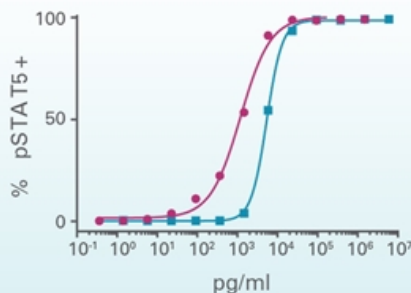
IL-2  $\beta/\gamma$  demonstrated strong receptor bias with reduced IL-2R $\alpha$  binding and well-retained IL-2R $\beta$  binding

# Receptor Selectivity Confirmed in Primary Human Cells

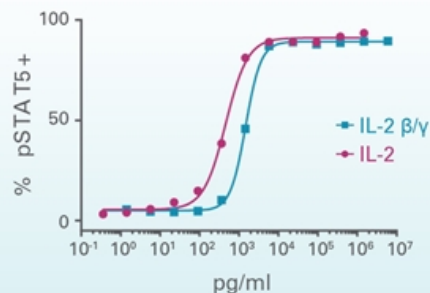
### Human Treg cells



### Human CD8<sup>+</sup> T cells



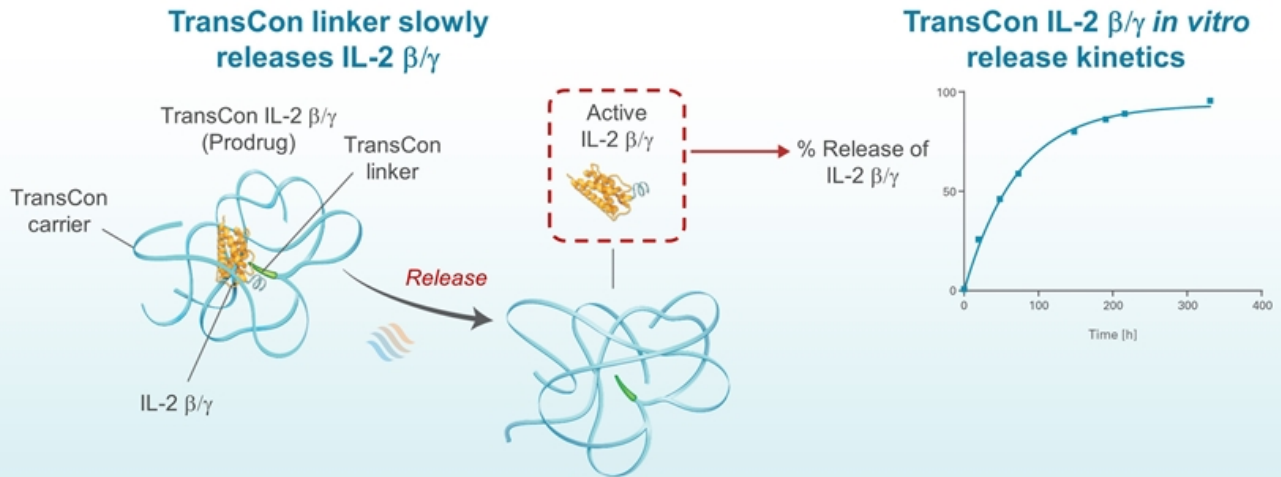
### Human NK cells



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

# Design of TransCon IL-2 $\beta/\gamma$ :

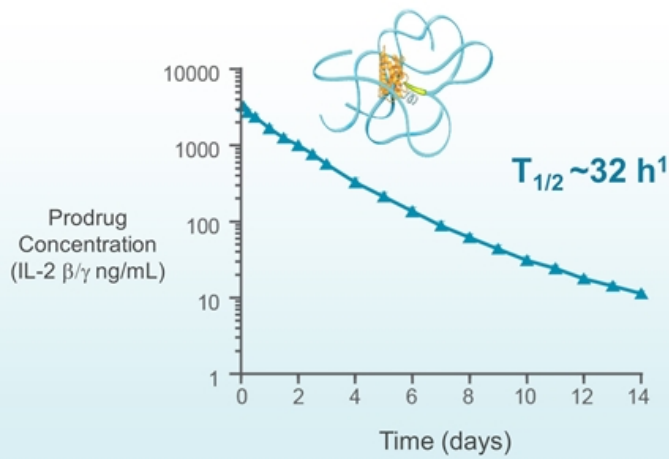
## 2) TransCon Technology to Optimize Exposure



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



# TransCon IL-2 $\beta/\gamma$ Resulted in Long-lasting Exposure in NHP



- TransCon IL-2  $\beta/\gamma$  plasma PK in NHP demonstrated prolonged, sustained release of IL-2  $\beta/\gamma$
- $T_{1/2}$  of TransCon IL-2  $\beta/\gamma$  prodrug and released IL-2  $\beta/\gamma^2$  was  $\sim 32 \text{ h}$

PK profile supports potential best-in-class properties

NHP = non-human primates.

<sup>1</sup>Rosen D, et al. AACR annual meeting, 2020; Poster 4507.

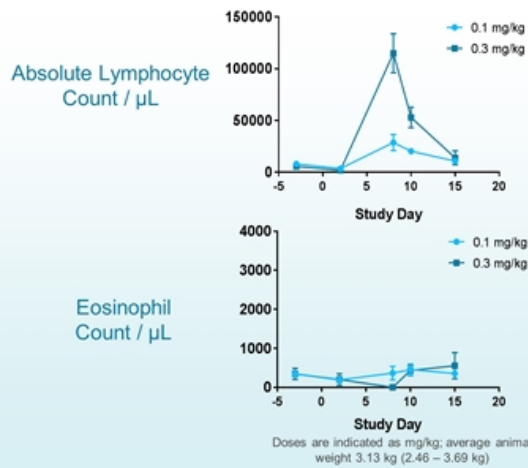
<sup>2</sup>Data on file.

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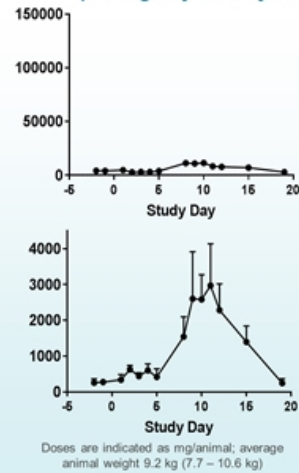
ascendis  
pharma

# Robust Increase in Lymphocyte Count with Minimal Eosinophil Expansion in NHP

**TransCon IL-2  $\beta/\gamma^1$**   
(Single Dose on Day 1)



**Aldesleukin<sup>2</sup>**  
(0.4 mg/day on Days 1-5)



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<sup>3,4</sup>

Q3W = every 3 weeks

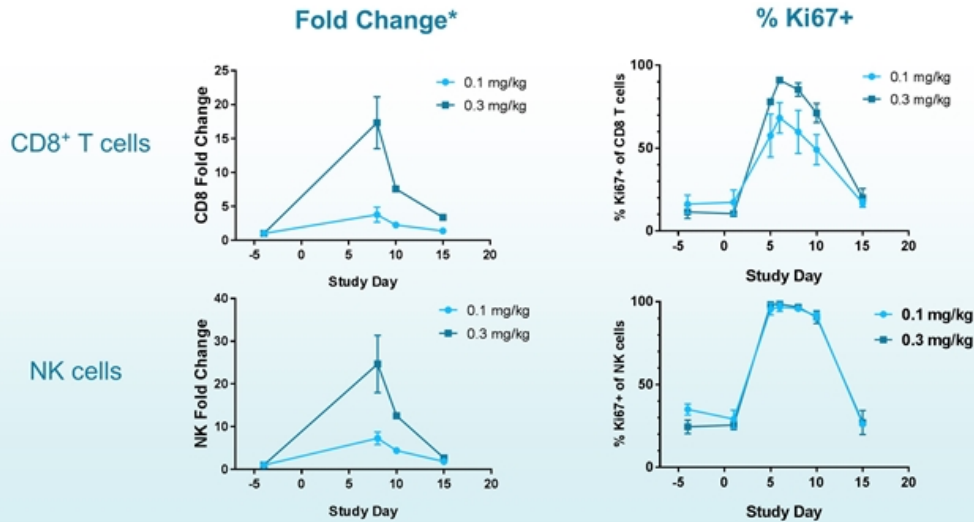
<sup>1</sup>Data on file. <sup>2</sup>Rosen D, et al. AACR annual meeting. 2020; Poster 4507.

<sup>3</sup>Rand, et al. *J Clin Invest.* 1991; 88: 825. <sup>4</sup>Van Haelst Pisanic C, et al. *Blood.* 1991;78:1538.

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# Potent CD8<sup>+</sup> T Cell and NK Cell Expansion and Activation in NHP

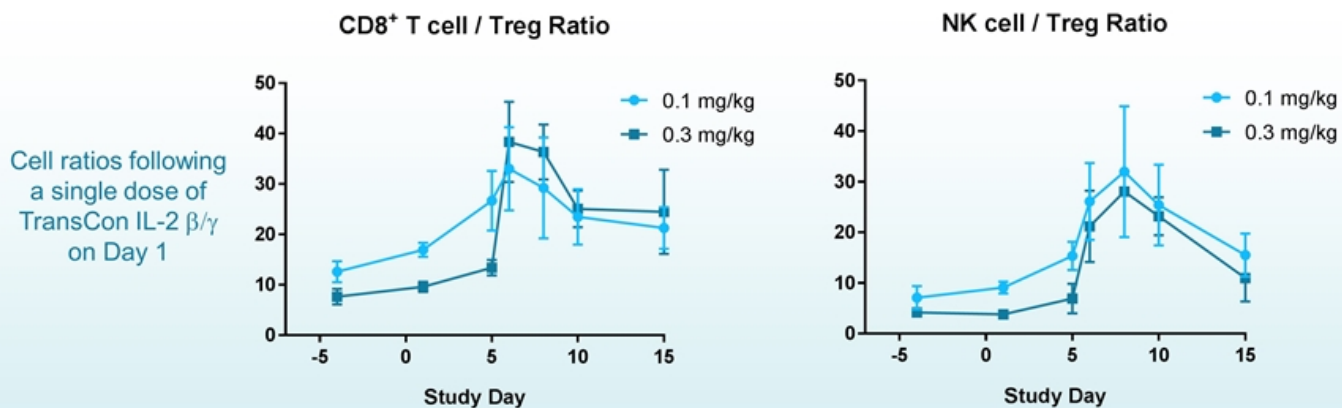


Expansion and activation of cytotoxic lymphocyte subsets observed following a single dose of TransCon IL-2  $\beta/\gamma$

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

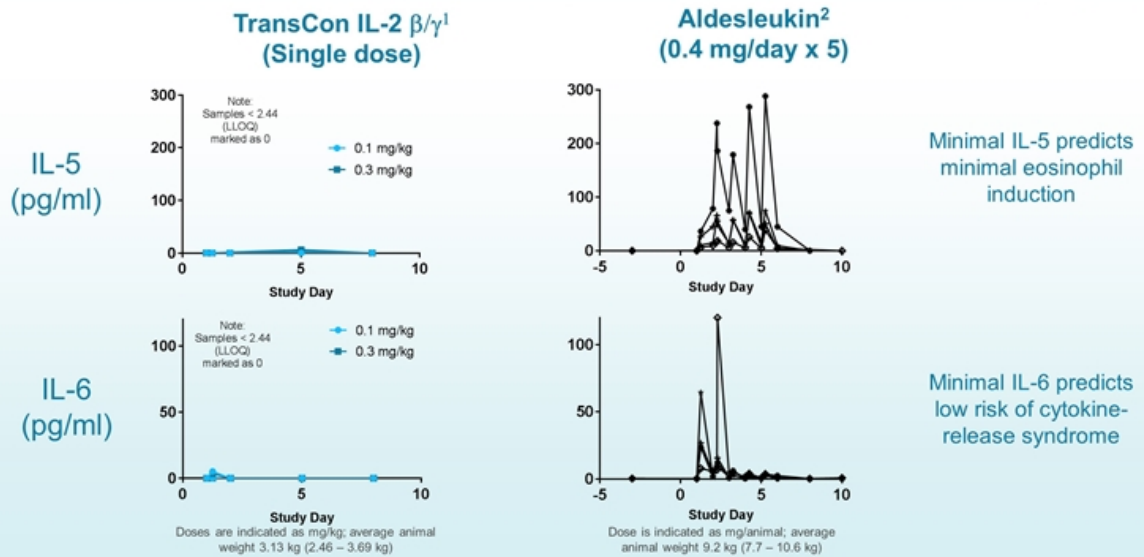
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# TransCon IL-2 $\beta/\gamma$ Expands Ratios of CD8<sup>+</sup> T Cells and NK Cells Over Treg Cells in NHP



Consistent with observed minimal binding to IL-2R $\alpha$ , the ratios of CD8<sup>+</sup> T cells and NK cells over Treg cells increased following administration of TransCon IL-2  $\beta/\gamma$  in NHP

# Single Dose TransCon IL-2 $\beta/\gamma$ Induced Lower Levels of Systemic Inflammation Markers in NHP When Compared to Aldesleukin



TransCon IL-2  $\beta/\gamma$  IND or similar expected in Q3 2021

# Evaluation of Immune Memory and Potential Cross-immunity Following TransCon IL-2 $\beta/\gamma$ plus TransCon TLR7/8 Agonist

Syngeneic CT26 tumor model  
(colon-derived tumor line)

Treatment with TransCon IL-2  $\beta/\gamma$   
+ TransCon TLR7/8 Agonist

Re-challenge of complete  
responders with CT26

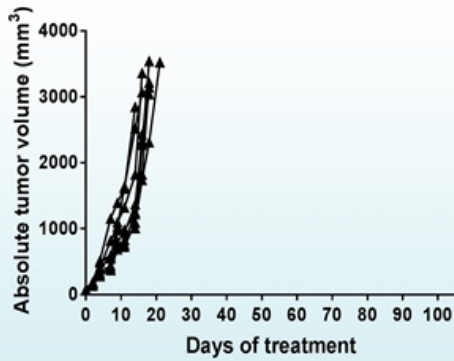
- 73 days after initial treatment
- No new treatment

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

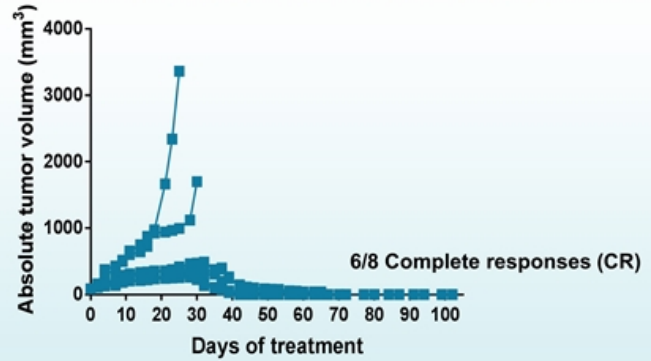
- 28 days after CT26 re-challenge
- No new treatment

# TransCon IL-2 $\beta/\gamma$ Plus TransCon TLR7/8 Agonist Resulted in Durable Complete Tumor Regressions in the CT26 Tumor Model

Buffer control



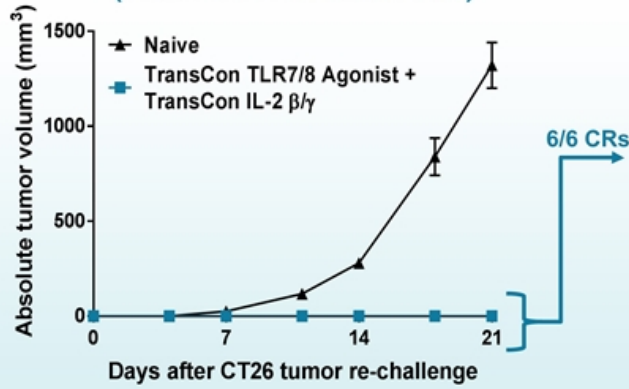
TransCon IL-2  $\beta/\gamma$  (3 doses) +  
TransCon TLR7/8 Agonist (single dose)



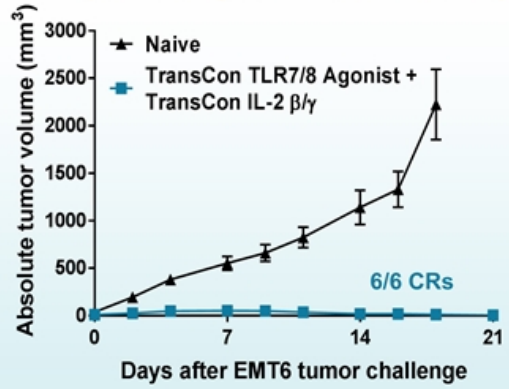
The immune activating mechanism of action of TransCon IL-2  $\beta/\gamma$  plus TransCon TLR7/8 Agonist and complete responses suggests potential for anti-tumor immune memory

# 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



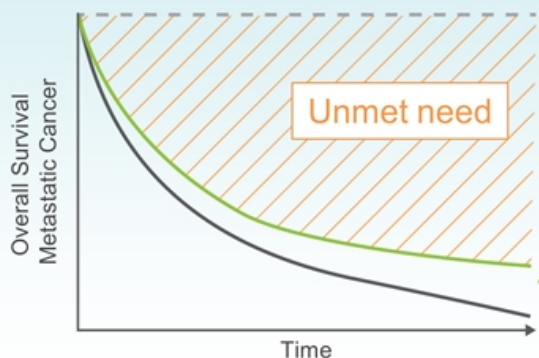
## Potential Paradigm Shift to How Cancer is Treated

- 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  $\beta/\gamma$  designed for IL-2R $\beta/\gamma$  selectivity, combined with low C<sub>max</sub> 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  $\beta/\gamma$  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

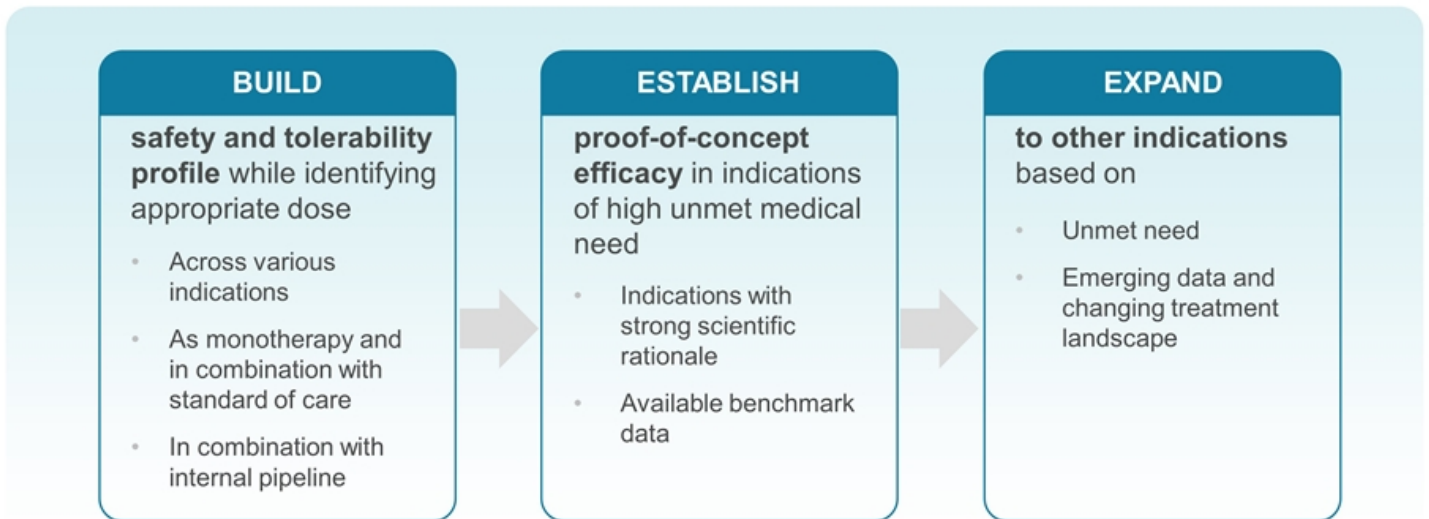


- U.S. cancer patients eligible for checkpoint inhibitors (CPI) increased from 1.5% in 2011 to 43.6% in 2018
- Percentage of patients estimated to respond to CPI was 0.1% in 2011 and increased to 12.5% in 2018

Immunotherapy has "raised the tail" for multiple tumor types

More effective therapies are urgently needed

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



# 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**

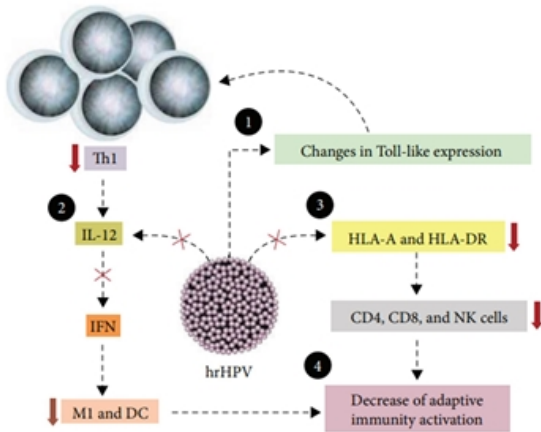
Multiple indication-specific  
cohorts at Recommended  
Ph2 Dose (RP2D)

**Objectives:**

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

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

## TLRs and HPV-associated cancers<sup>1</sup>



## 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+<sup>2</sup>

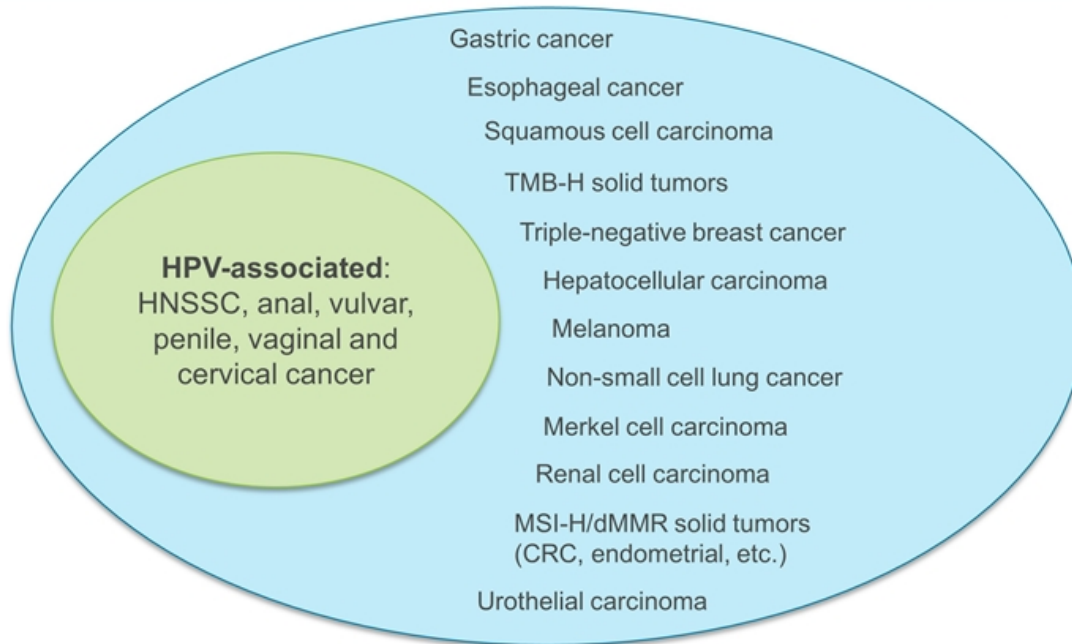
**Anal, cervical, vulvar, penile, vaginal:** vast majority (>70-90%) are HPV+

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

51 | <sup>1</sup>Barros M, et al. *J Immunology Res.* 2018; 2912671:1-17.  
<sup>2</sup>Mahal B, et al. *Cancer Epidemiol Biomarkers Prev.* 2019; 10:1660-1667.

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

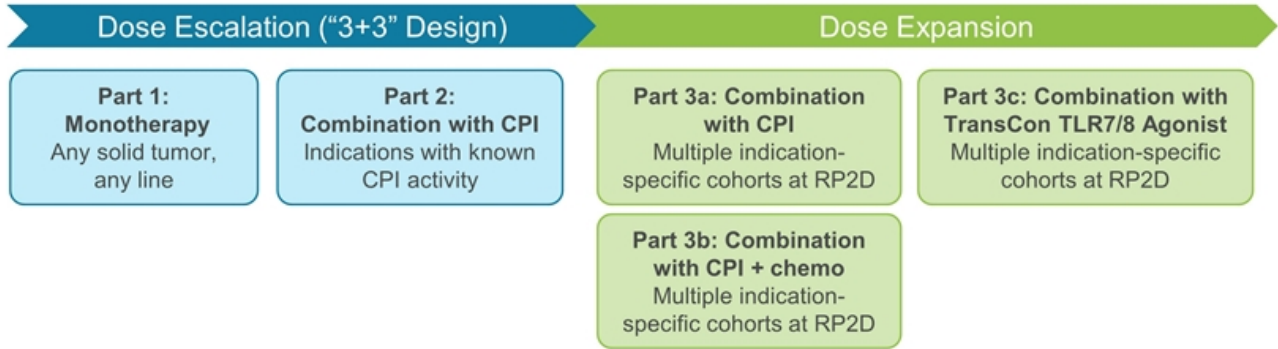


## TransCon TLR7/8 Agonist - Summary

- 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 $\beta/\gamma$ 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 $\beta/\gamma$ – Potential Backbone Agent in Oncology

- TransCon IL-2  $\beta/\gamma$  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  $\beta/\gamma$ 
    - Potential to become a backbone agent in oncology
    - IND or similar expected TransCon IL-2  $\beta/\gamma$  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