Antibody directed IL-2 for tumor immunotherapy

Non-Confidential Introduction

July 2020

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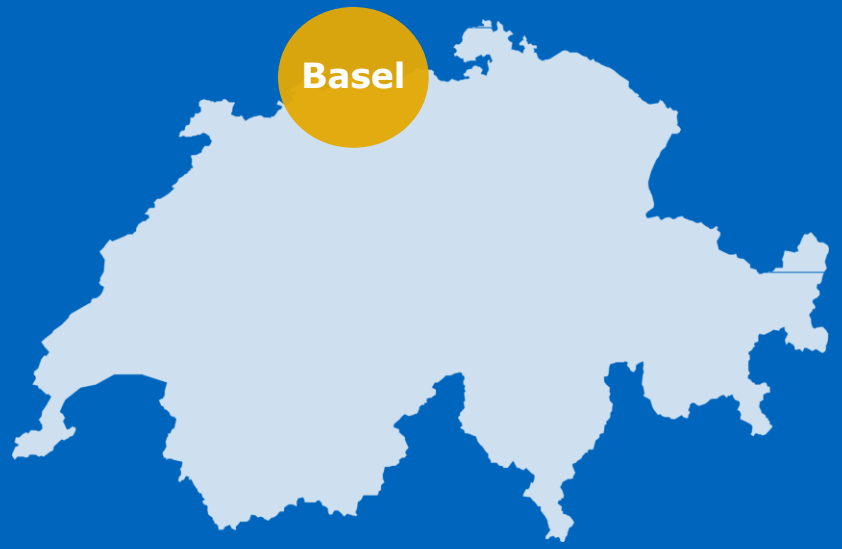


Anaveon is a spin-out of University of Zurich and Novartis, founded in Switzerland in 2017 by leading experts in the field of immunotherapy

Vision:
Use our expertise in cutting-edge immunology to design and develop patient treatments that benefit society

Company highlights

Lead program is ANV419, a highly potent fusion protein of an IL-2 and an anti-IL2 antibody that is redirected toward the β/γ receptor

ANV419 improves on Proleukin's efficacy and limitations with a more selective and safer product profile

ANV419 selectively promotes IL-2 signalling to immune effector cells, and limits signalling to immune regulatory cells and non-immune cells, in mice and NHPs

ANV419 has demonstrated proof of concept in mice tumor models

Anaveon is well positioned to be best in class in the field of engineered IL-2 and therapeutic cytokines

Differentiated preclinical profile for ANV419, with strong IP and freedom to operate

Follow-up targeted compounds in early pre-clinical stages

Anaveon is moving quickly to the clinic with fast timeline to demonstrate differentiation

Single-arm, multiple-indication Phase 1/2 study for ANV419 on track to start in Q1 2021

Potential for synergistic combination of ANV419 with multiple anti-cancer modalities

Well funded and backed by a world-class team

Syncona

NMF
FUNDED BY NOVARTIS

CHF 35M Series A

UZH Life Sciences Fund

CHF 1M convertible loan

BASELAUNCH

CHF 150 K award

Who we are

Management

Andreas Katopodis, PhD
Chief Executive Officer

Co-founder of Anaveon with 26 years' experience at Novartis and Ciba-Geigy. He was instrumental in many aspects of early to late drug development for immune mediated diseases, such as solid organ transplantation and autoimmunity.

Christoph Huber, PhD
Chief Scientific Officer

Over 10 years' experience in drug R&D in cancer immunotherapy and vaccines, inflammation, asthma, and immuno-safety. Before joining Anaveon, he held leadership positions at Roche, Pfizer, and COI Pharmaceuticals.

Christoph Bucher, MD
Chief Medical Officer

Over 8 years' experience in early clinical drug development in immunology and stem cell transplantation at Roche and Novartis. He still practices Hematology part time at the University Hospital of Basel.

Board

Martin Murphy, PhD
Chairman
CEO, Syncona Investment Management Ltd

Allison Jeynes, MD
Independent Director
CEO, Avillion LLP

Dominic Schmidt, PhD
Partner, Syncona Investment Management Ltd

Florian Müllershausen, PhD
Managing Director, Novartis Venture Fund

Alice Renard, PharmD
Observer
Partner, Syncona Investment Management Ltd

Anja König, PhD
Observer
Global Head, Novartis Venture Fund

Scientific advisors

Jane Osbourn, PhD
Chair of cell therapy company Mogrify, CSO of Alchemab Therapeutics

Robert Hawkins, MD
CEO of Immetacyte Ltd, Hon. Professor of Medical Oncology at the University of Manchester / Christie Hospital

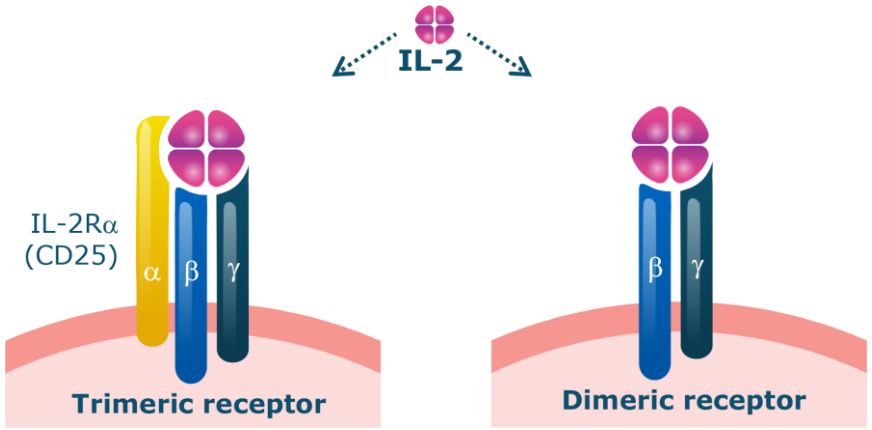
Wolf-Hervé Fridman, MD
Emeritus Professor of Immunology at the University of Paris

IL-2 is a key regulator of anti-tumor biology

IL-2 is a key component of immune response to tumors

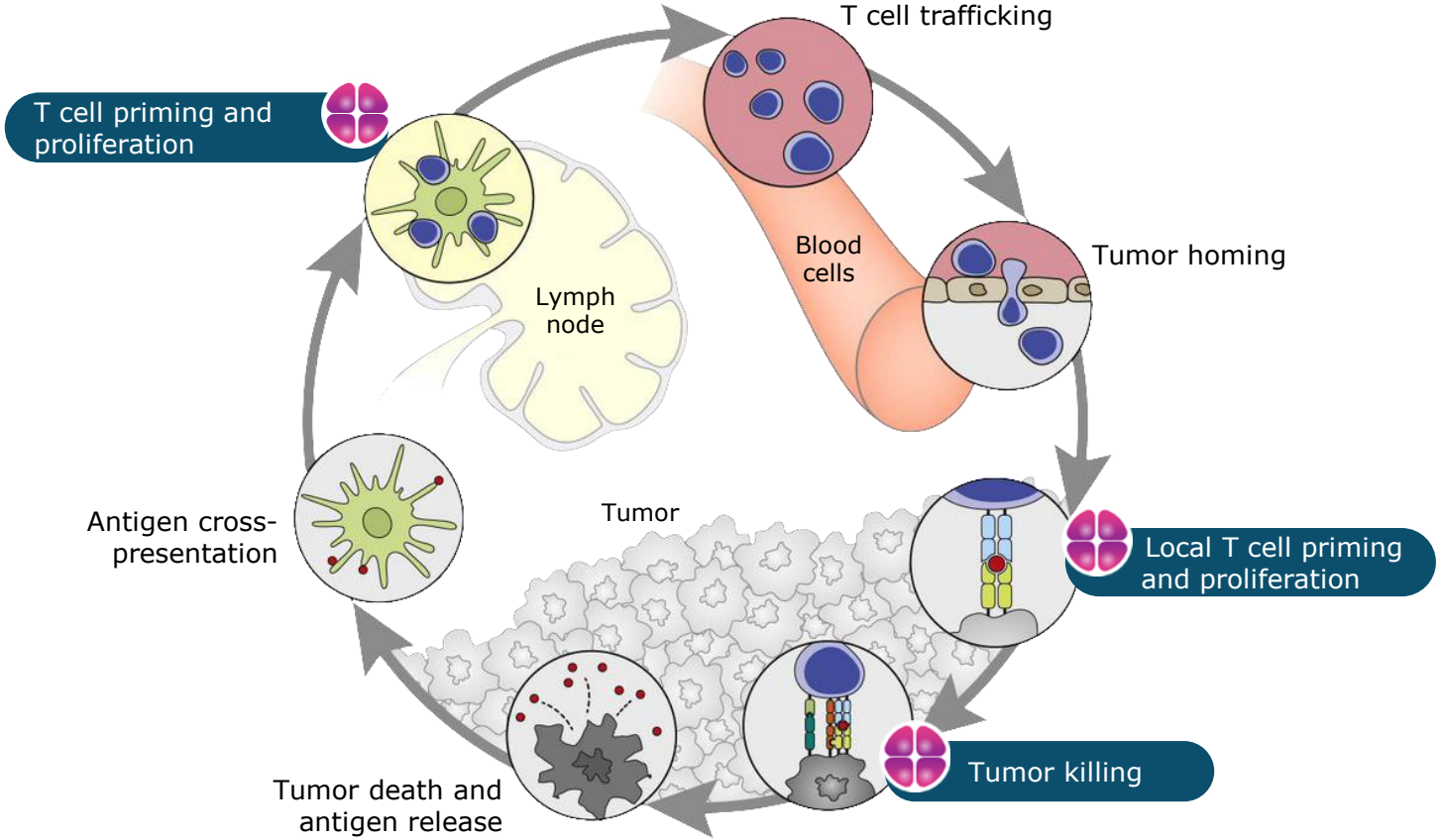
- IL-2 acts on immune cells (including effector and regulatory T cells, NK cells)
- Tumor immunotherapy success correlates with restoration of CD8+ T cell function

IL-2 acts through two receptor configurations



- $CD4^+$ regulatory T cells (Treg) limit anti-tumor responses
- Pulmonary endothelial cells contribute to dose limiting toxicity

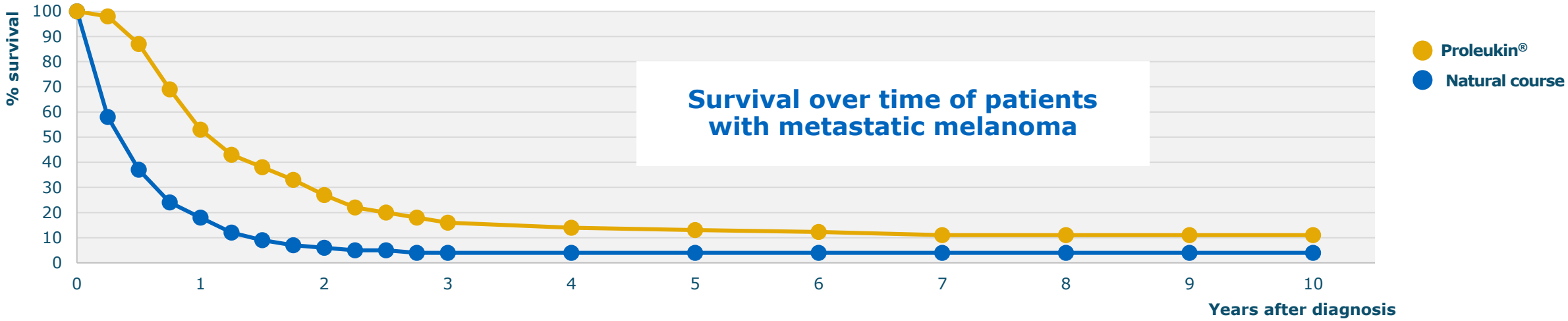
- $CD8^+$ T cells
- NK cells promote anti-tumor responses



Graphic adapted from Chen & Mellman; Immunity (2013)

The first wave of IL-2 immunotherapy treatment and PROLEUKIN®

Proleukin® (recombinant IL-2) is approved for metastatic melanoma and RCC



But Proleukin® has many limitations restricting its use

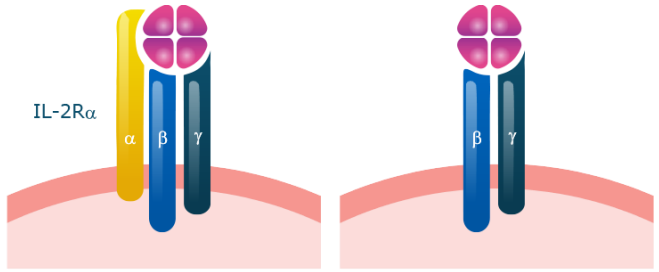
- Low therapeutic index (proliferation of both effector and Treg cells)
- Toxicity, notably vascular leak syndrome (due to multiple target cells)
- Burdensome dosing schedule (due to poor pharmacokinetics and administration in hospital)

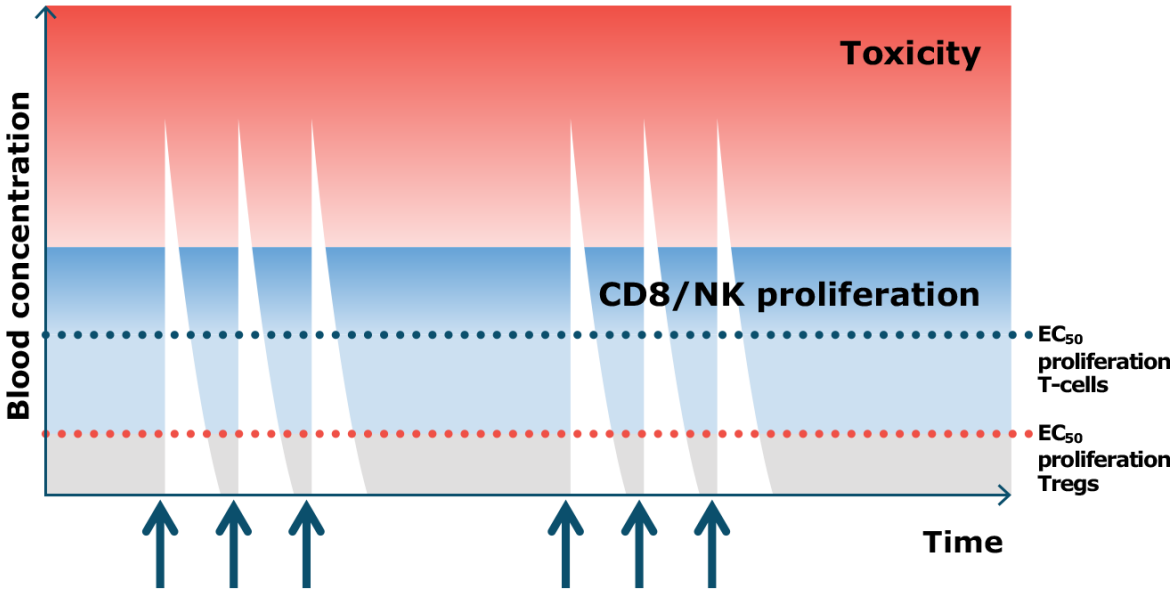
Proleukin® resulted in >10 year survival in 14% of metastatic melanoma patients, highlighting the potential of IL-2 agonists to induce long-term remission in cancer patients

Haffner et al. Brit J Cancer (1992) 66, 856; Smith et al. Clin Cancer Res (2008) 14, 5610v

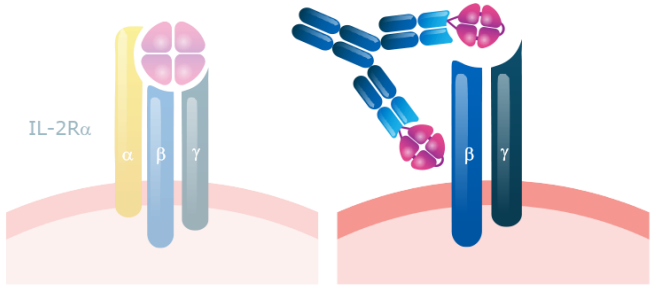
From PROLEUKIN® to ANV419

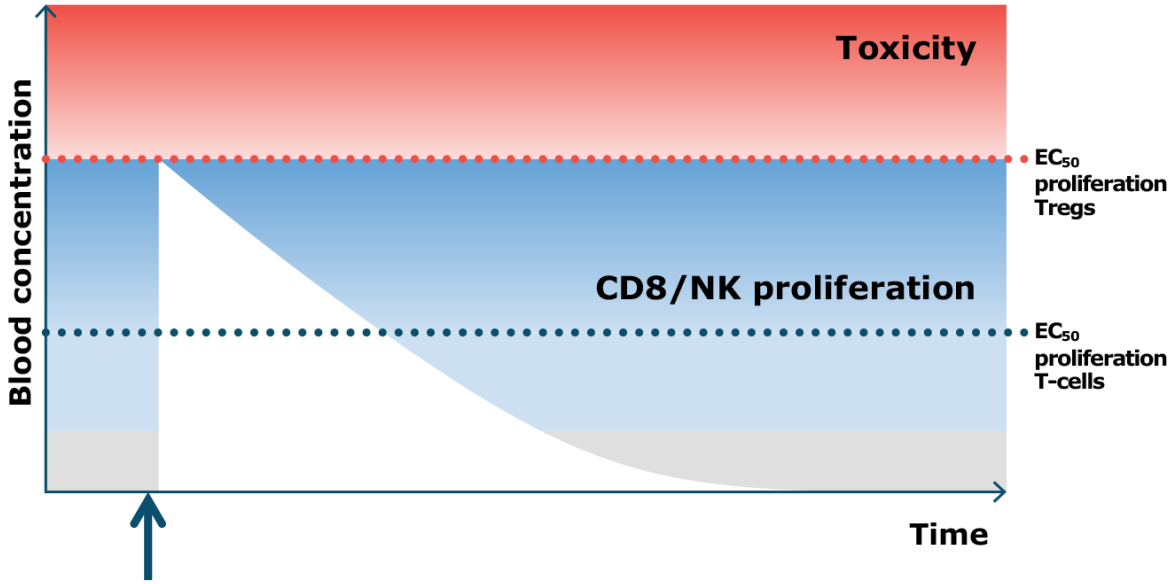
Proleukin®
Signals through:





ANV419
Signals through:

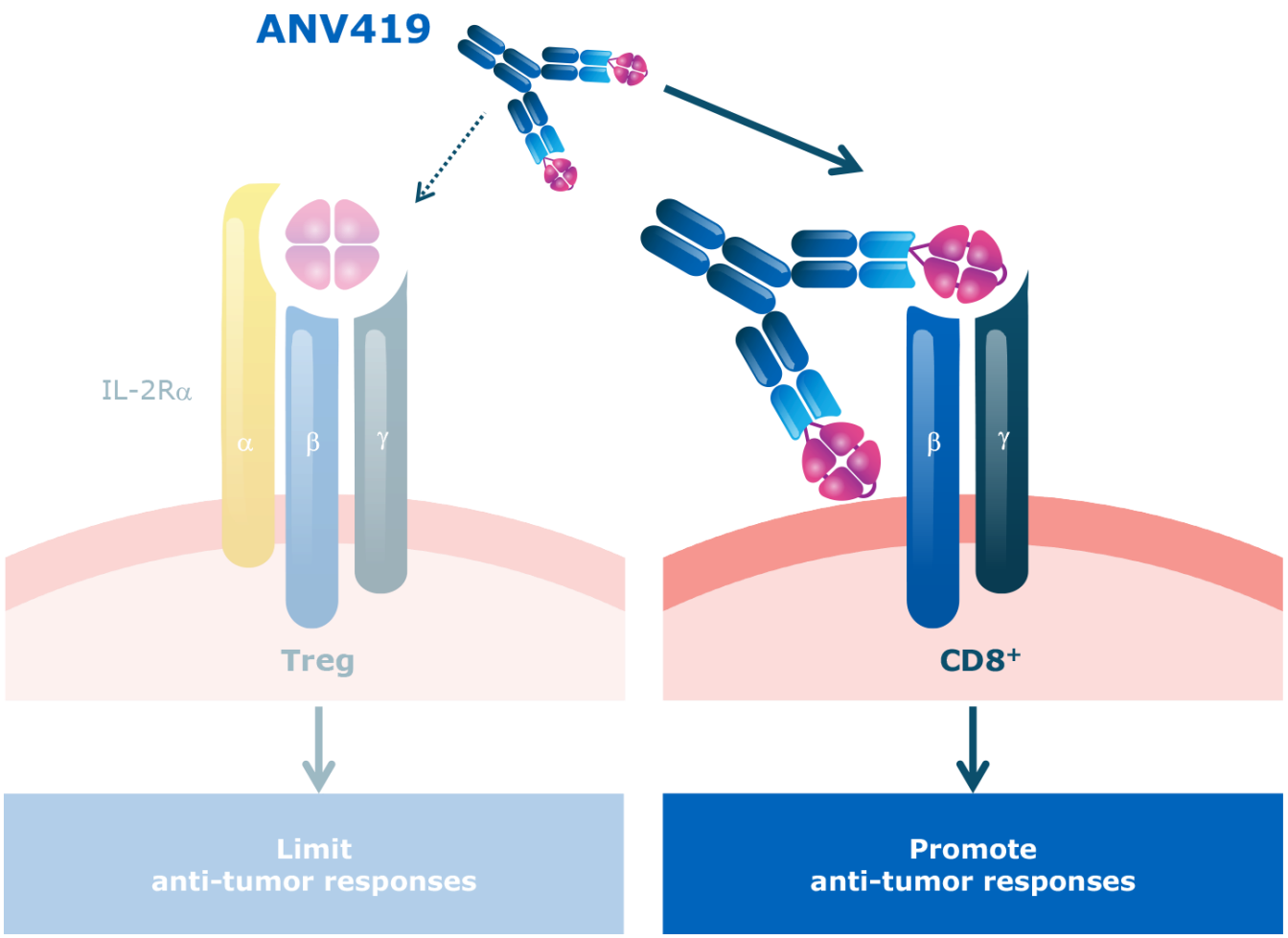




☒ **Lack of selectivity**
Dose-limiting toxicity
Short *in vivo* half-life

☑ **Excellent selectivity for effector cells**
Good therapeutic window
Extended half-life

ANV419 is a leading next-generation IL-2



ANV419 is a fusion protein of IL-2 and an anti-IL-2 antibody which specifically blocks IL-2Rα binding

This strategy allows redirection of IL-2 to the dimeric receptor without the mutations and inherent unknows of IL-2 "muteins"

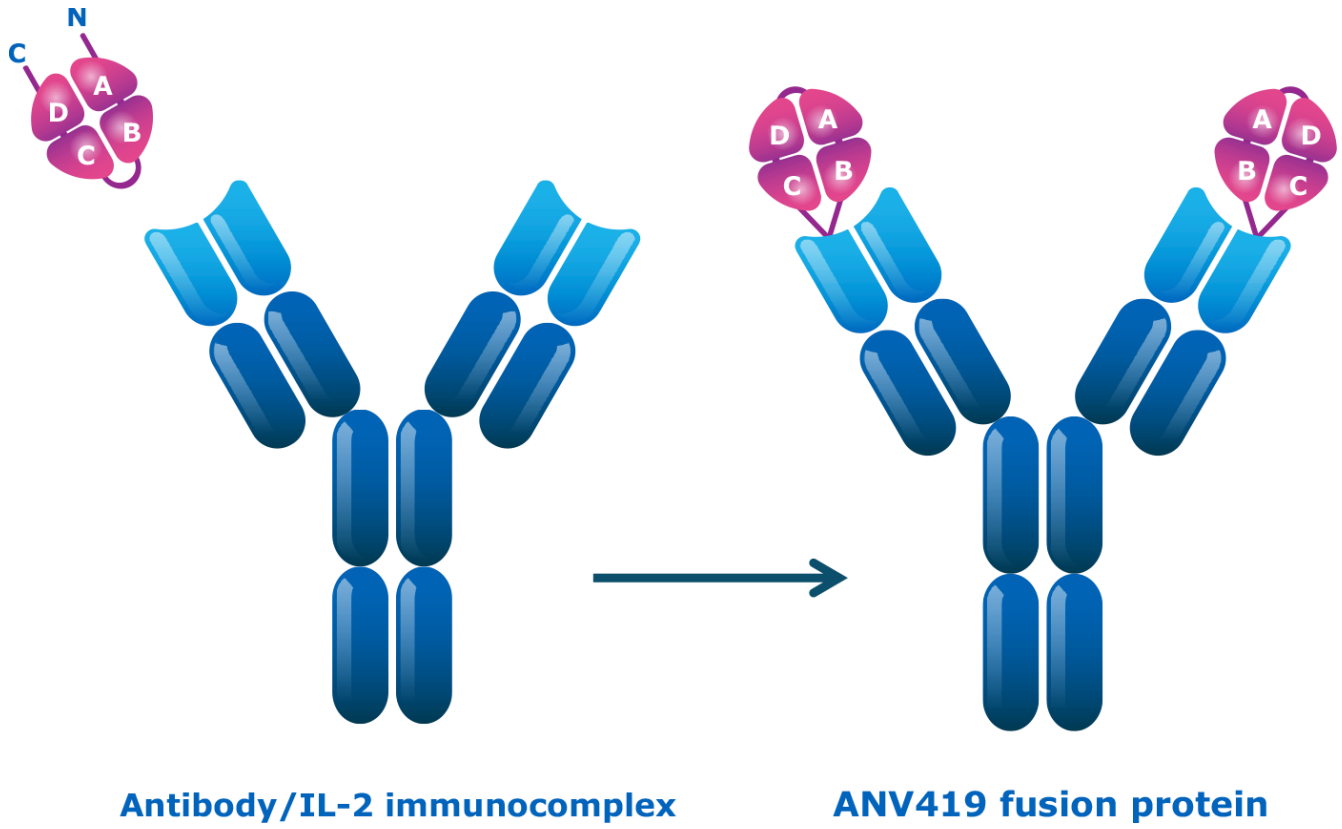
ANV419 properties support a best-in-class profile:

1. Selectively blocks the IL-2/IL-2Rα interaction
2. Selectively stimulates effector over regulatory cells, to improve efficacy
3. Improved safety and therapeutic index

ANV419 is selective by design

ANV419 was designed to selectively redirect IL-2 in three steps:

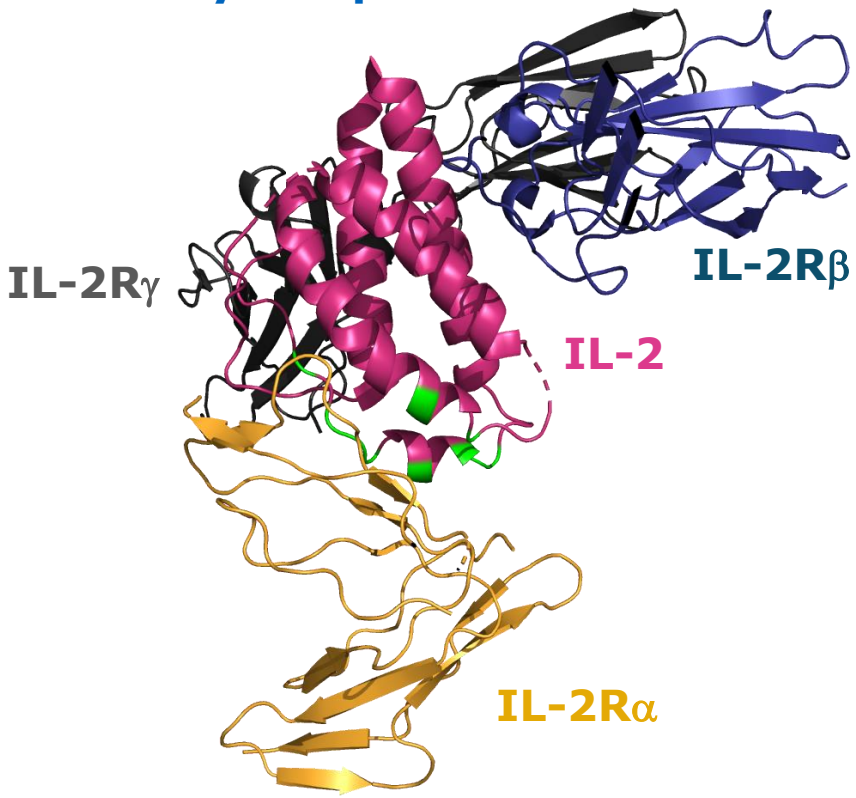
- Generation of anti-IL-2 antibodies
  - Highly specific antibodies were selected to permit binding to IL-2Rβ/γ and block binding to IL-2Rα
- Selection of the lead antibody
  - Optimal pharmacodynamic and pharmacokinetic properties (affinity and off-rate)
  - Humanisation
- Fusion of the antibody and IL-2
  - Cut & Join strategy: cutting IL-2's B-C loop, followed by trans-ligation of IL-2 with the CDR portion of the antibody, and joining of the N- and C-termini of IL-2



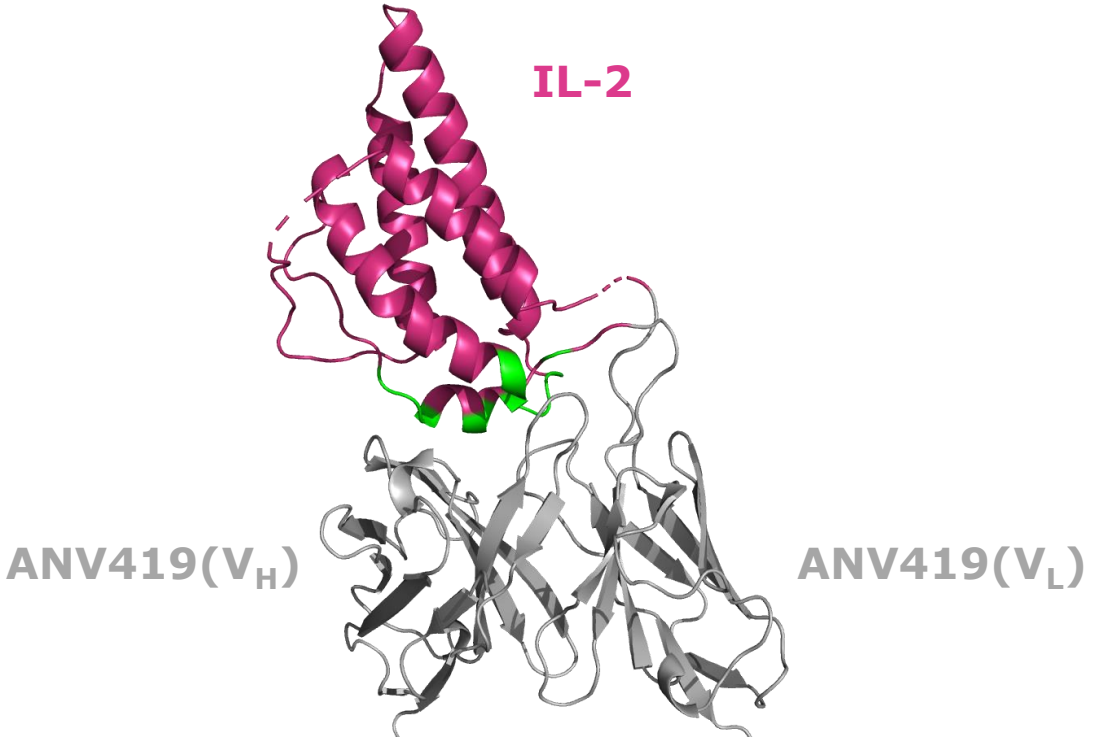
Antibody/IL-2 immunocomplex **ANV419 fusion protein**

ANV419 selectively allows binding to IL-2Rβ/γ by interfering with IL-2Rα

Crystal structure of the IL-2/IL-2R tertiary complex



Crystal structure of ANV419 (including IL-2 component)

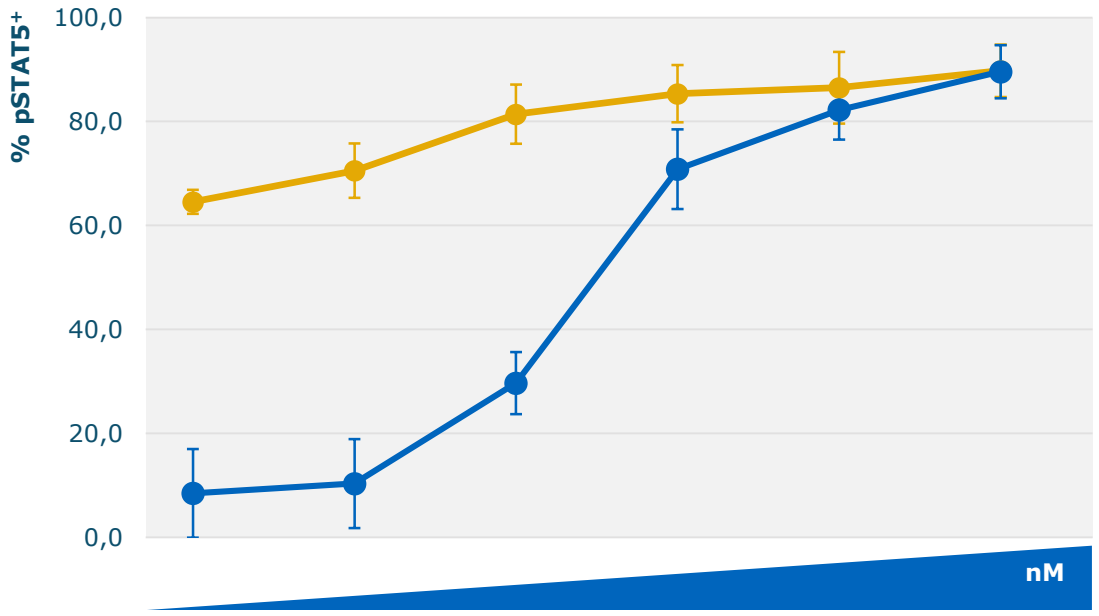


ANV419 maintains the same key intramolecular contacts with IL-2 as IL-2Ra (shown here in green)

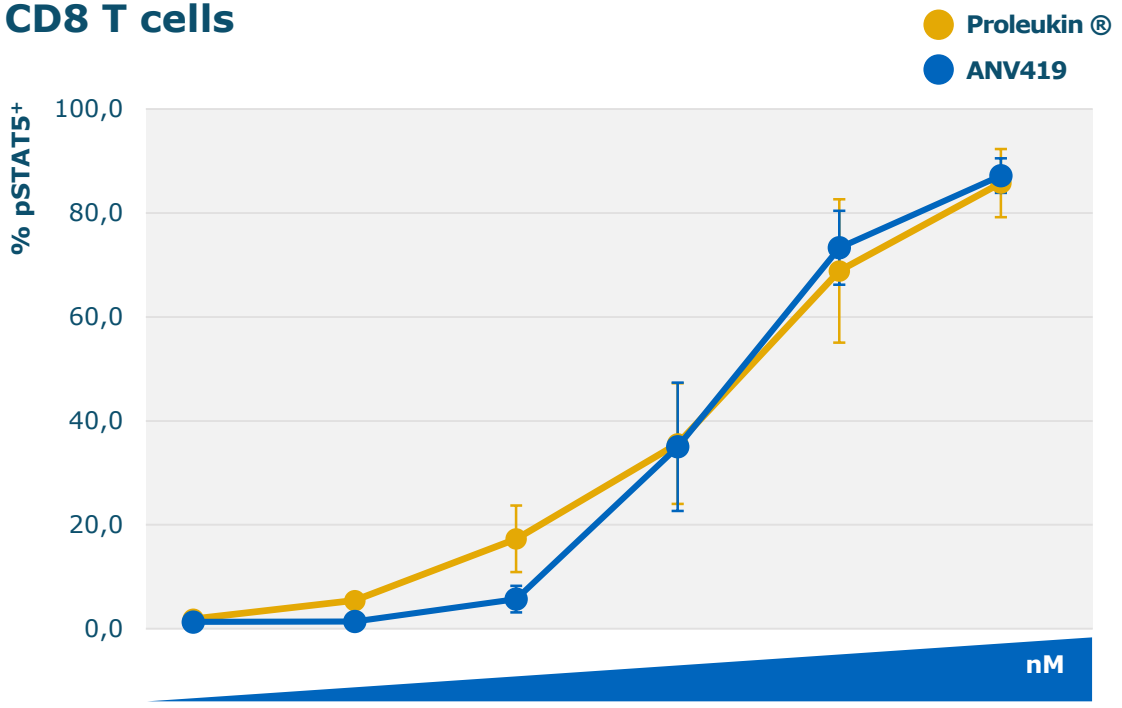
ANV419 demonstrates selectivity for human CD8 T cells vs. Treg

In vitro triggering of IL-2 receptor signalling on human Tregs and CD8 T cells by ANV419 as measured by pSTAT5 analysis

Tregs



CD8 T cells



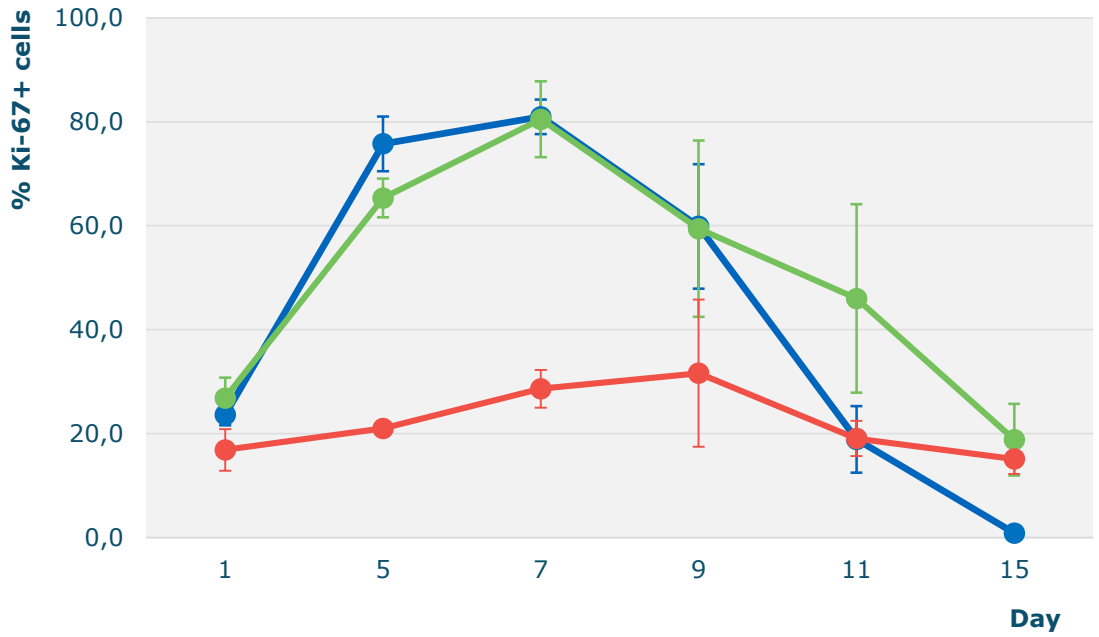
ANV419 has much reduced potency for IL-2 receptor triggering in Tregs while maintaining full potency in CD8 T cells

Human peripheral blood mononuclear cells were treated for 10 min. with different concentrations of Proleukin® or ANV419 and cells were analyzed by fluorescence-activated cell sorting (n=3 donors)

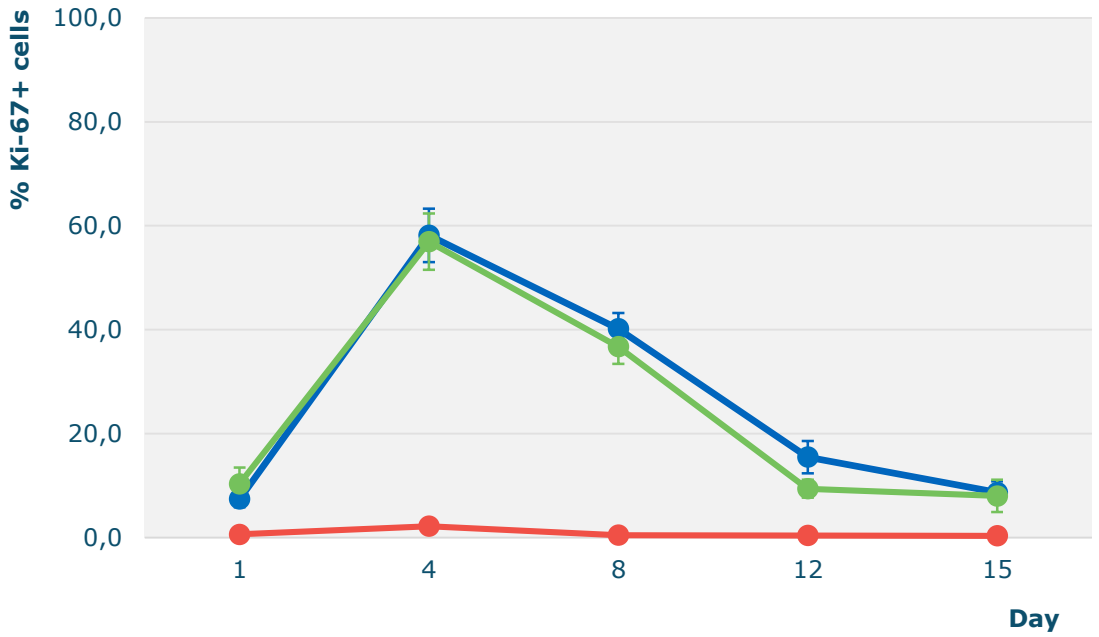
ANV419 selectively promotes CD8 T and NK cells vs. Treg cells, in mice and non-human primates

CD8 T cells
NK cells
Treg cells

In Mice



In NHP



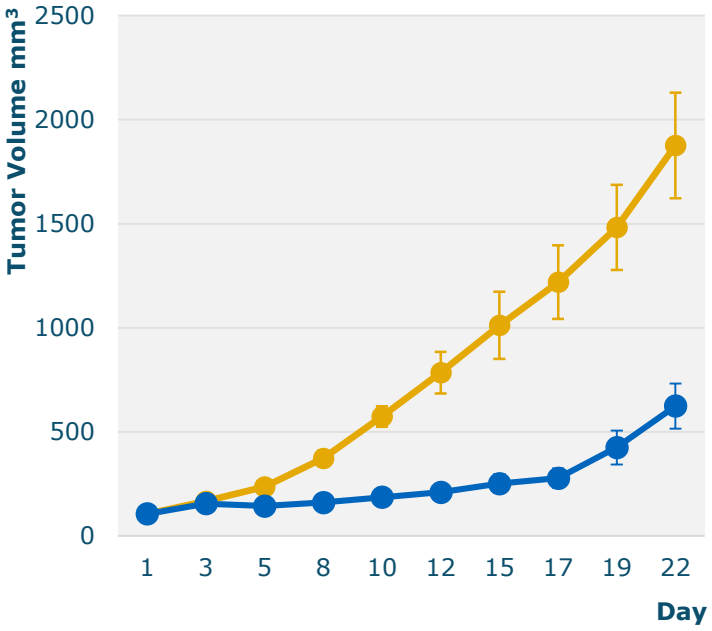
***In vivo* selective induction of proliferation marker Ki-67 in effector cells but not in Tregs**

Mice and NHPs injected with ANV419 on day 1 and bled for immunophenotyping at the specified day post injection (n=3 animals)
Graphs depict % of cell subset expressing Ki67 in the blood.

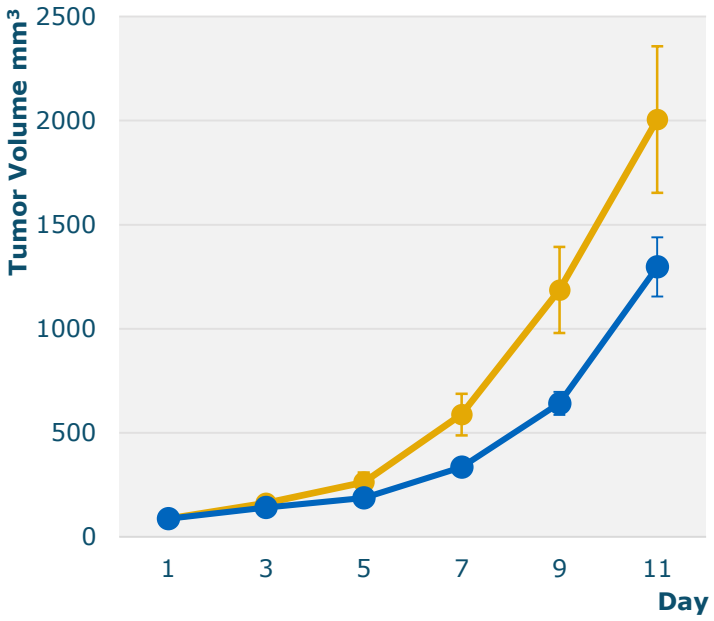
ANV419 inhibits tumor growth in mouse models

ANV419
Vehicle

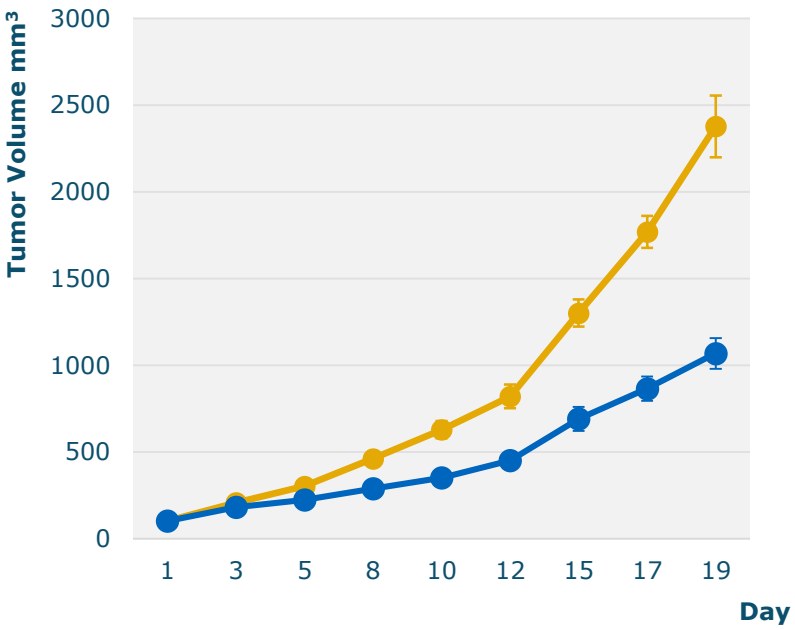
H22
Liver cancer model



B16F10
Melanoma model



Renca
Renal cell carcinoma model



ANV419 inhibits tumor growth in checkpoint inhibitor sensitive (H22) and resistant (B16F10, Renca) tumor models

Mice injected on Day 1 and sacrificed at the specified day post injection.
Graphs depict % of cell subset expressing Ki67 in the blood.

ANV419 is long acting and has a favorable safety profile in NHPs

ANV419 has a very good safety profile at multiples of the expected maximal human dose in NHPs

- Maximal dose tested was 6x expected effective dose in human
- Dose-dependent exaggerated pharmacology typical for IL-2 was observed in the highest-dose group only (with no severely toxic events observed)
- Exaggerated pharmacology syndrome was observed in fewer organs and to a lesser degree compared to Proleukin®

No eosinophilia is observed up to the highest dose tested

No vascular leak syndrome was observed in NHPs at all doses tested, despite 1 min i.v. infusion

- Comparable doses of Proleukin® cannot be infused i.v. due to toxicity
- Likely best in class vs. competitors with regard to infusion reaction and tolerability

ANV419 behaves like an antibody, with extended in vivo effects. These properties are likely to result in best in class usage and safety profile.

High level comparison of novel IL-2 modalities

	Stage	Partnered	Selectivity *in vivo* (for CD8, NK cells)	Long half-life	Safety	Low risk for immunogenicity
NKTR-214 (Nektar)	Phase 3	BMS	✗	✓	✓	✓
THOR707 (Synthorx/Sanofi)	Phase 1/2	Sanofi	✗	✗	✓*	✓
KY1043 bispecific (Kymab)	Preclinical	No	✗	?	?	✗
RG7461 bispecific (Roche)	Phase 1/2	NA	✗	✓	✓*	✗
NL-201 (Neoleukin)	Preclinical	No	?	✗	?	✗
MDNA19 (Medicenna)	Preclinical	No	✓	✗	✓*	✗
ALKS-4230 (Alkermes)	Phase 1/2	No	✓	✗	?	✓
ANV419 (Anaveon)	Preclinical	No	✓	✓	✓*	✓

ANV419 matches all the requirements for a next-gen IL-2 better than the competition

*Preclinical data in Non-Human Primates

ANV419 is selective for IL-2Rβ

Affinity of ANV419 to IL-2R α and β was determined by Biacore

	K_D IL-2Rα (CD25)	K_D IL-2Rβ (CD122)
ANV419	No binding	377 nM
IL-2 (published)	10 nM	~500 nM
NKTR-214 (1-PEG)[1]	190 nM	1770 nM
THOR-707[2]	No binding	>IL-2
Neo-2/15[3]	No binding	11 nM
MDNA19[4]	No binding	2 nM

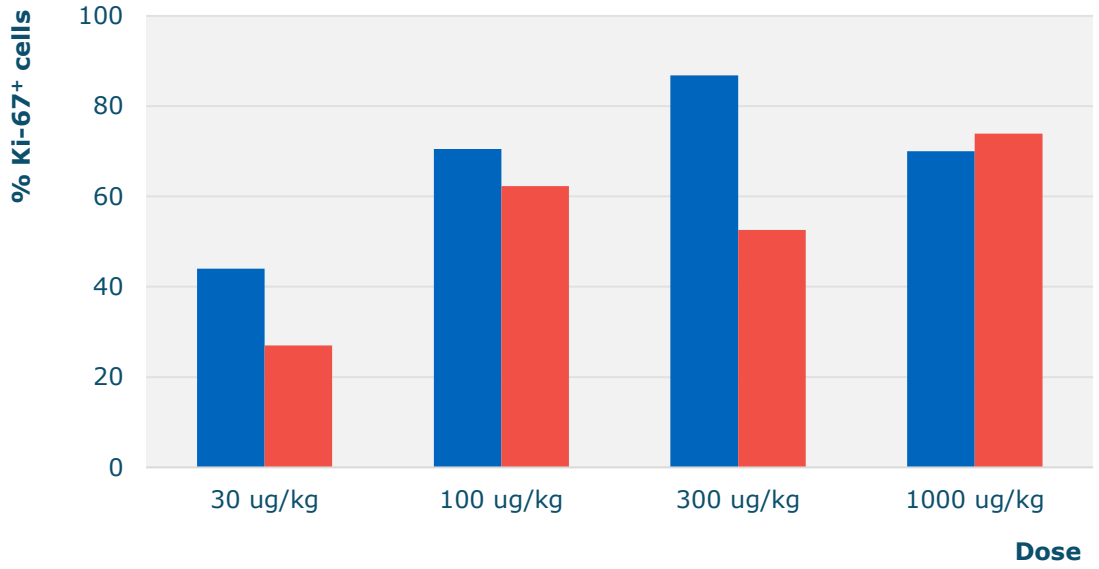
→ ANV491 does not bind to IL-2R alpha and retains binding to IL-2R beta with affinity comparable to IL-2

[1]Charych et al. PLOS ONE (2017); [2]Mitta et al. SITC (2018); [3]Silva et al. Nature (2019); [4]Medicenna corporate presentation (2020)

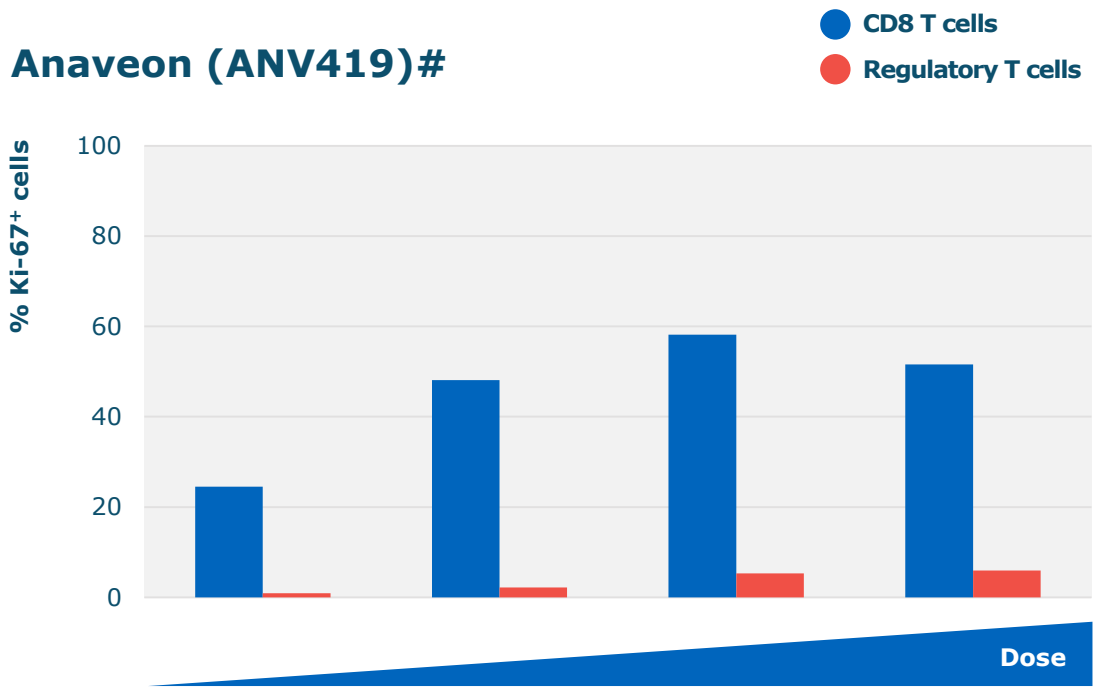
Example of Anaveon's best-in-class selectivity in non-human primates

Comparison of proliferation in peripheral blood, %Ki-67 in CD8 T cells and Tregs at peak day

Synthorx (THOR-707)*



Anaveon (ANV419)#



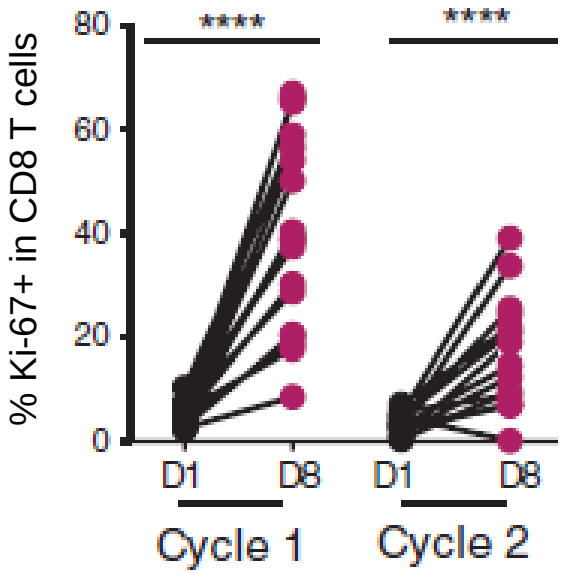
ANV419 has better *in vivo* selectivity for CD8 T cells than THOR-707

* Non-human primate data from ASCO 2019 poster
\# Non-human primate data from two independent studies (n=3 in each group)

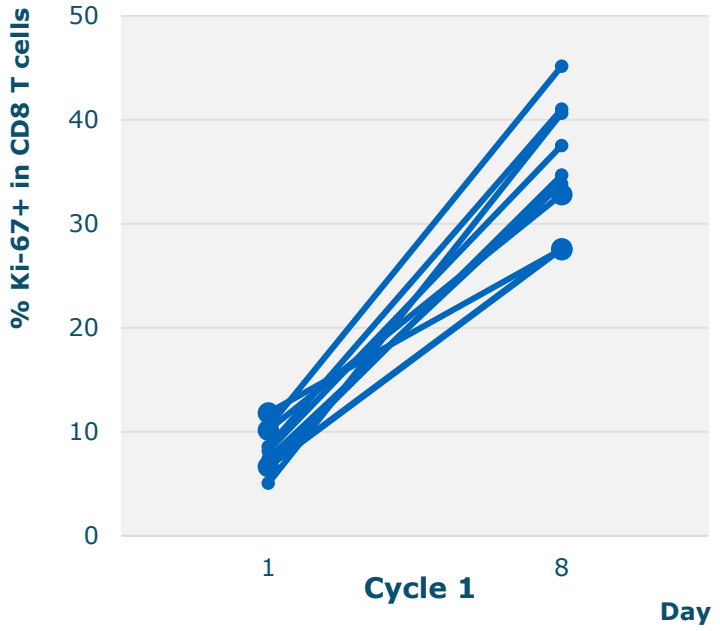
Example of Anaveon's best-in-class selectivity in non-human primates

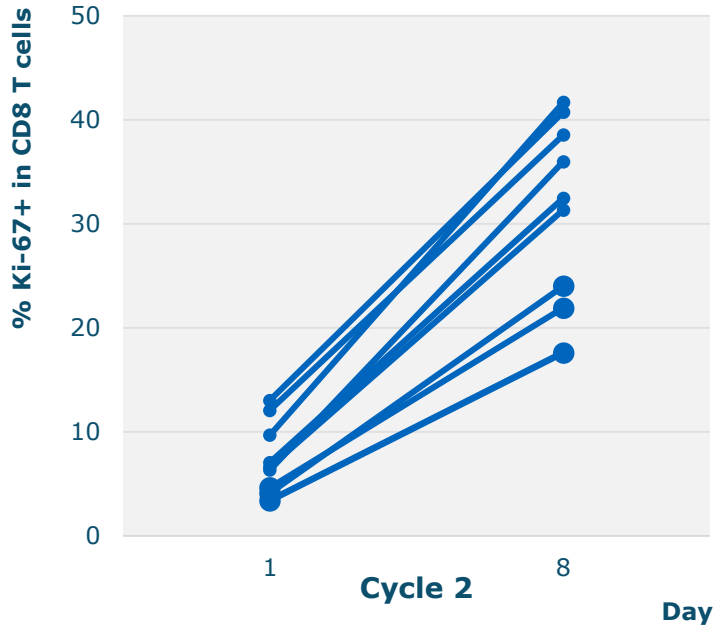
Comparison of CD8 T cell proliferation in peripheral blood

Nektar (NKTR-214)*



Anaveon (ANV419)#





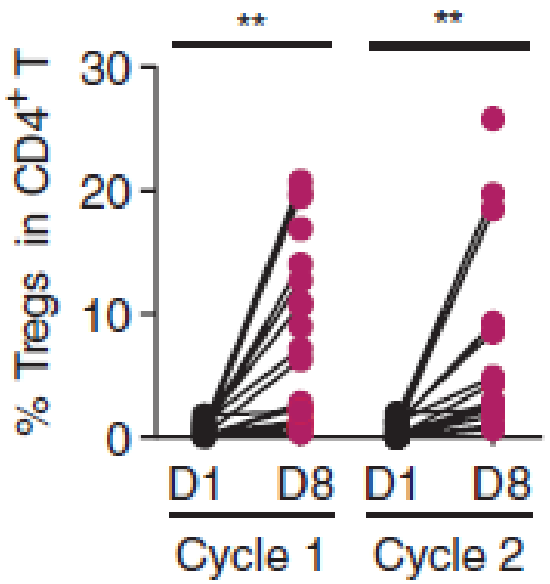
ANV419 induces proliferation of CD8 T cells

* Nektar FIH publication, Cancer Discov. 2019 Jun;9(6):711-721
\# Non-human primate data combined from 3 dose levels

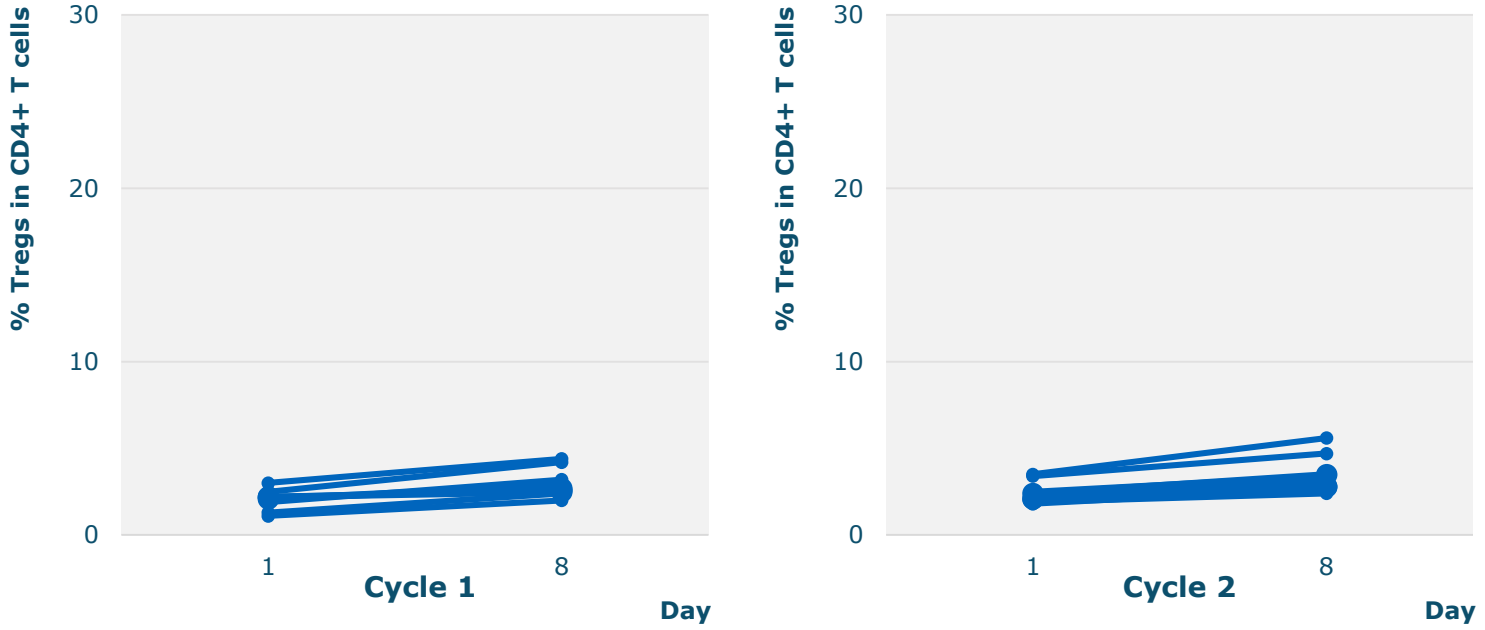
Example of Anaveon's best-in-class selectivity in non-human primates

Comparison of Treg expansion in peripheral blood

Nektar (NKTR-214)*



Anaveon (ANV419)#

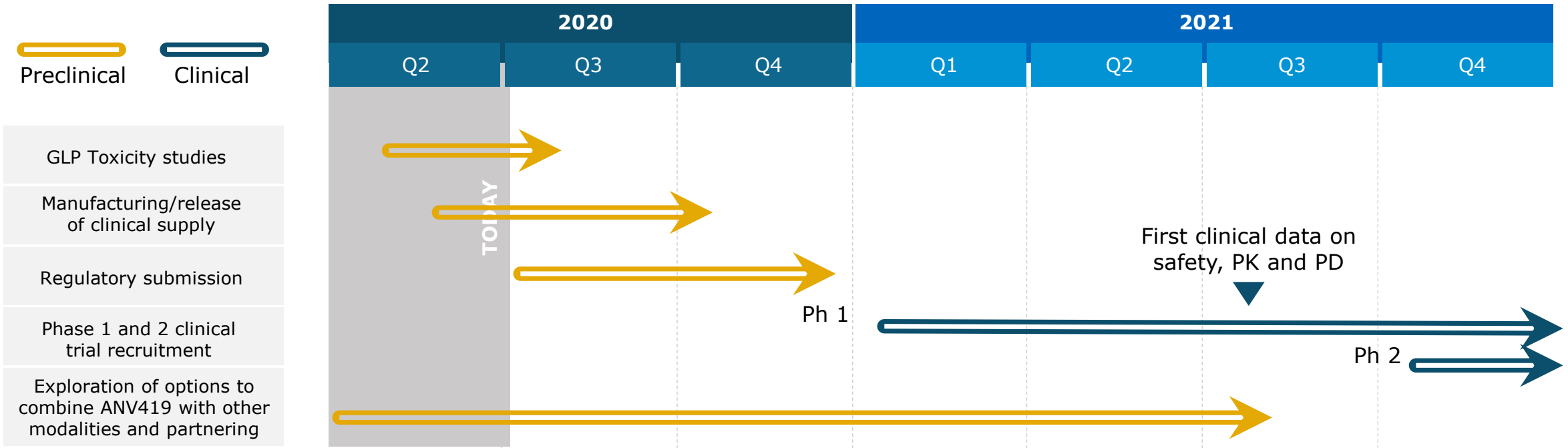


ANV419 does not expand Tregs in peripheral blood

*Nektar FIH publication, Cancer Discov. 2019 Jun;9(6):711-721
#Non-human primate data combined from 3 dose levels with at least 40% Ki-67+ CD8 T cells

Anaveon's route to the clinic

Lead candidate ANV419 selected | ANV419 proof of concept in NHPs | CMC feasibility completed



Fast timelines to the clinic and quick demonstration of ANV419's differentiated profile

Manufacturing/CMC and Clinical Supply

Excellent yields and purity at cell culture level

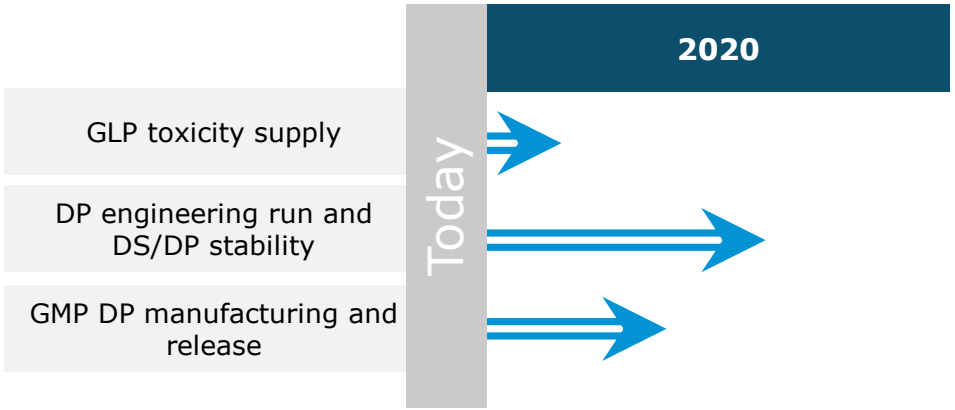
- Upstream culture conditions have been optimized and locked

Downstream purification yields high drug substance (DS) recovery

- Purification process fully optimized and locked

ANV419 behaves like an antibody, increasing predictability in CMC

Successful formulation completed, and long term stability of drug product (DP) is ongoing



Clinical supply on target for first-in-man submission in Q4 2020

ANV-419 Clinical Development Plan

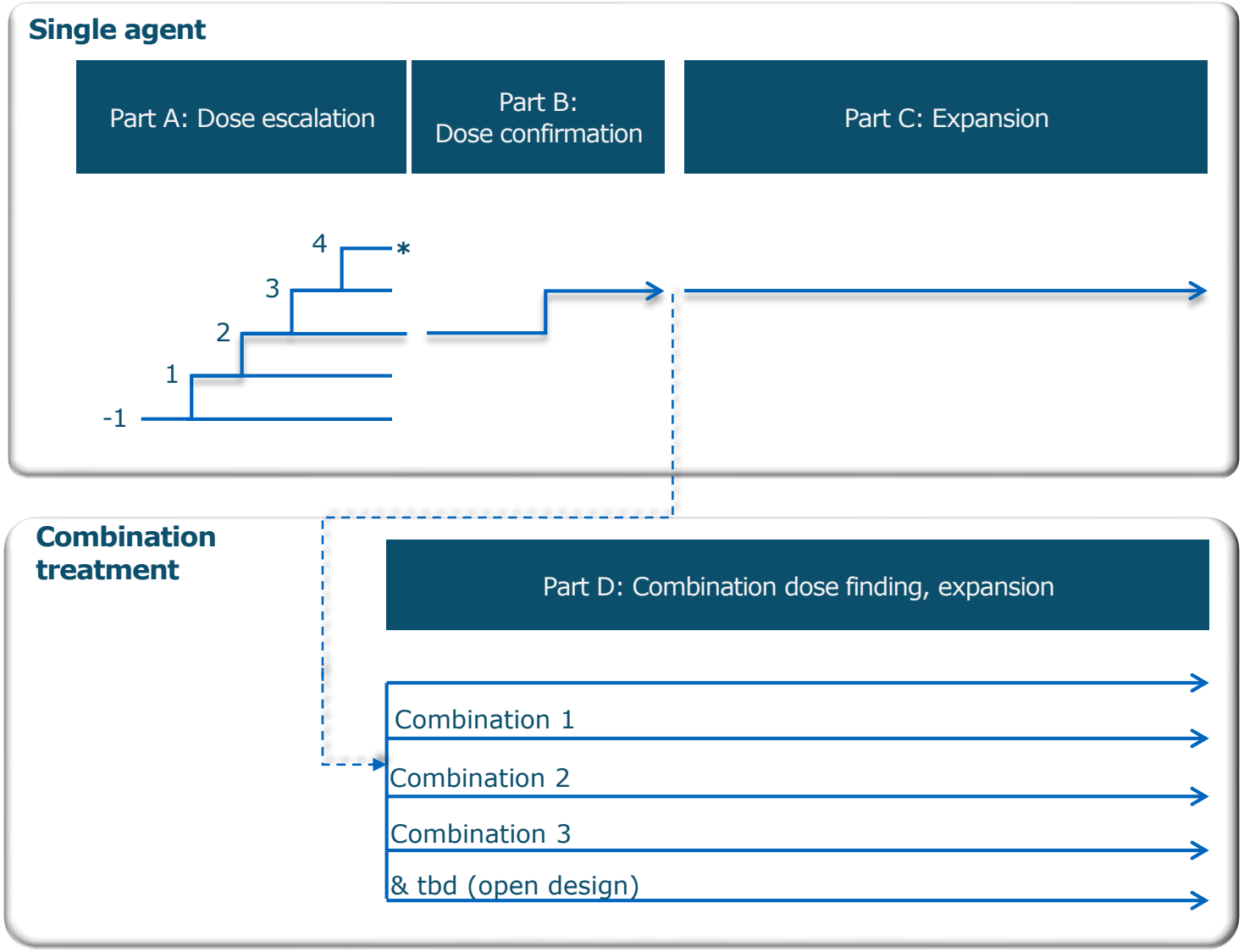
Leveraging available data on target, pathway and PK/PD

Optimize time and patient number towards recommended phase 2 dose

- ANV419 NHP and *in vitro* data will be combined with within-class human *in vitro* and clinical data to help minimize the number of dose levels used in First-in-Human study
- Safety confirmed by SRC after each dose/cohort and blood biomarkers will be used for dose-escalation guiding.
- After first DLT part B will be triggered and 3+3 design will continue until MTD is reached

Early combination testing

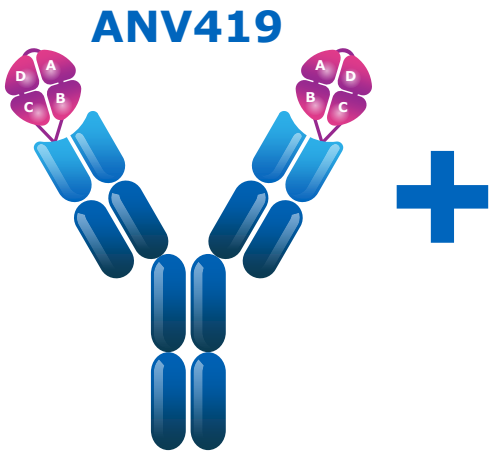
- Goal is to explore various mechanisms in a open design that will allow add-on of additional arms as combination partners and combination rationale become available
- By testing 2 different PD-1 inhibitors broad applicability of ANV-419 & CPI approach can be established



Exploration of Combination Options for ANV419

ANV419 has the potential to be combined with multiple anti-cancer modalities

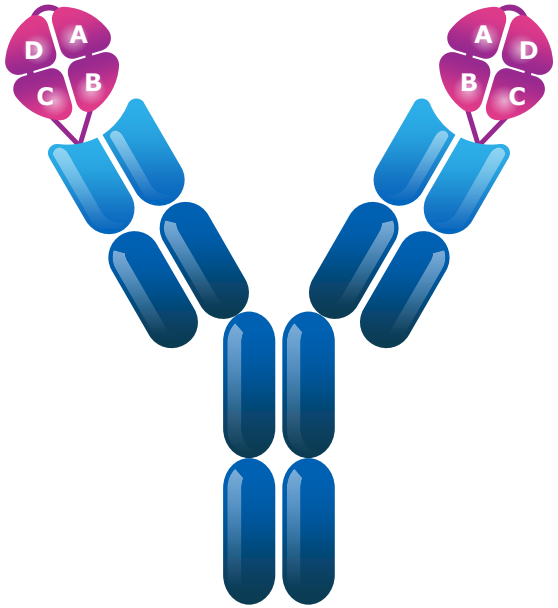
Multiple licensing and partnership opportunities



Combination agents	Potential applications
Checkpoint inhibitors	Melanoma, renal cell cancer, bladder cancer
Innate immunity agonists (TLR, STING agonists)	Solid tumors
Targeted agents (e.g. kinase inhibitors, EZH2 inhibitors, etc.)	Non-small cell lung cancer, MDS
CAR-T therapies	Hematological malignancies
TIL therapies	Melanoma
Antibodies HER-2, VGEF directed	Breast cancer, lung cancer, cervical cancer
Cytotoxic agents and radiation therapy	Conventional Chemotherapy Head and neck tumors
Immunization therapies	Solid tumors

Why Anaveon

ANV419



Next-generation biased IL-2 agonist with best-in-class potential

Excellent cell line productivity and protein stability, straight-forward and fast pre-clinical development program

Sterically blocks IL-2Rα engagement while maintaining strong signalling through the IL-2Rβ/γ

Systemic therapy with potential to be a safe and effective booster of the immune system in multiple tumor immunotherapy settings (either in monotherapy or in combination)

Selective signalling with strong proliferation of CD8+ T cells and NK cells, without proliferation of regulatory T cells, in mice and NHPs

Second generation ANV419 based compounds with targeted biodistribution are in early pre-clinical development for specific cancer indications

Extended *in vivo* half-life and strong pharmacodynamic effects, suggestive of infrequent dosing in humans

Entering first-in-human studies in Q1 2021

Thank you