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CONTROLLING INFLAMMATION

CORPORATE PRESENTATION

January 2022

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InflaRx N.V.

Targeting Complement to Control Inflammatory Diseases

☆ LEAD PRODUCT CANDIDATE WITH PIVOTAL PROGRAM FOCUS ON IMMUNODERMATOLOGICAL DISEASES

Clinical Efficacy and Clean Safety Profile enabling Vilobelimab to Advance in Multiple Indications

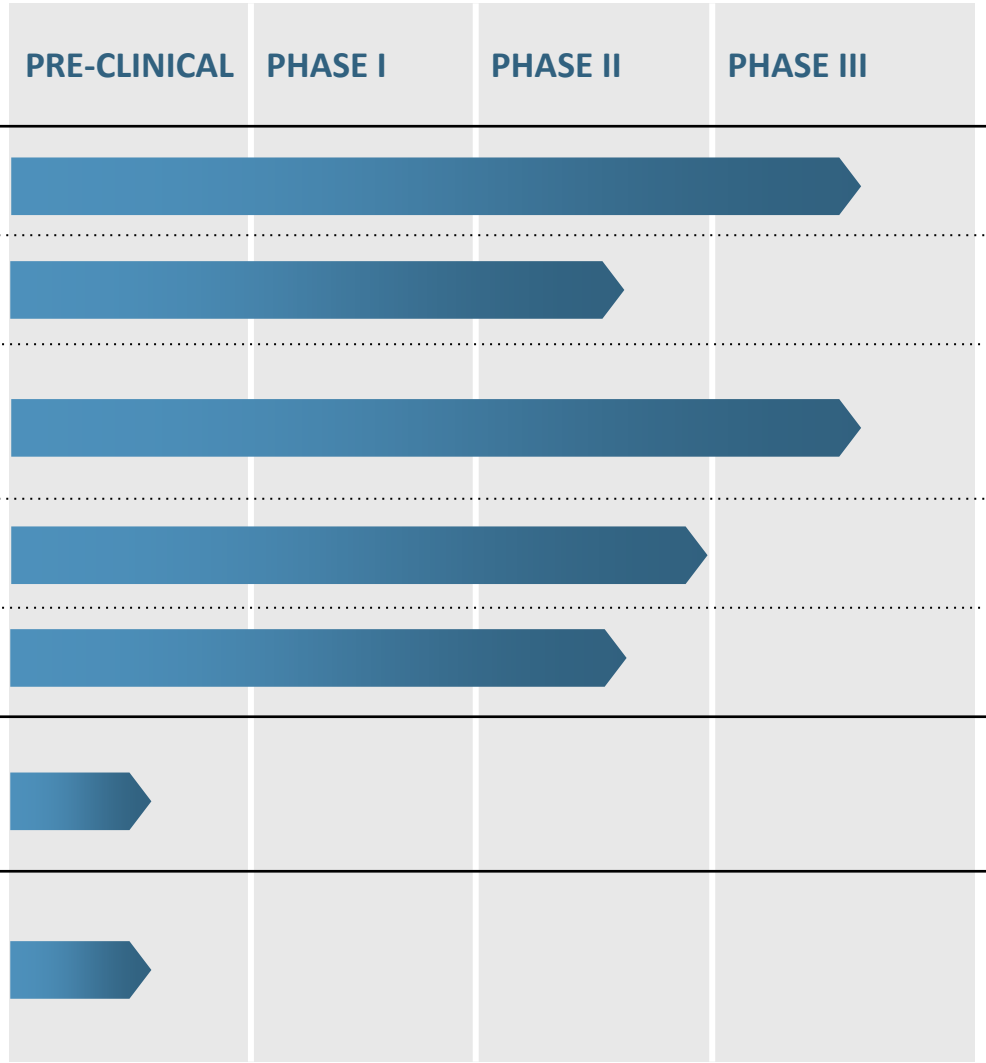
- **Hidradenitis Suppurativa (HS):** Initiated **pivotal study program in Q1 2022** after receiving no comments from the FDA in the 30-day review period
- **Pyoderma Gangraenosum (PG):** Positive Phase IIa data reported – gathering regulatory input on next steps for a pivotal program
- **Severe COVID-19:** Phase III enrollment completed; **topline data expected in Q1 2022**
- **ANCA-associated vasculitis (AAV):** Positive Phase II data enabling further development
- **Cutaneous squamous cell carcinoma (cSCC)**: Phase II study ongoing

New Program: Oral C5aR Inhibitor INF904 to Enter Clinic in H2 2022

- INF904 shows promising activity and clean safety profile in animals
- Best-in-class potential
- US patent issued in October 2021

Pipeline with Multiple Opportunities

	FRANCHISE	INDICATIONS	UPDATE
Vilobelimab ***C5a Inhibitor***	Immunodermatology	Hidradenitis Suppurativa (HS)	Pivotal trial initiated with new primary endpoint
		Pyoderma Gangraenosum (PG)	Positive preliminary Phase IIa open label results
	Life-threatening Inflammatory Diseases	Severe COVID-19	Phase II/III study: Phase II results published; Phase III fully enrolled, topline data expected Q1 2022
		ANCA-Associated Vasculitis (AAV)	Positive data in two Phase II trials
	Oncology	Cutaneous Squamous Cell Carcinoma (cSCC)	Phase II trial ongoing: first patient dosed in June 2021
IFX002 ***C5a Inhibitor***	Undisclosed Chronic Inflammatory and Autoimmune Diseases		Developing for optimized use for other chronic inflammatory indications
INF904 Oral ***C5aR inhibitor***	Undisclosed Chronic Inflammatory and Autoimmune Diseases		First-in-human study to be initiated in H2 2022



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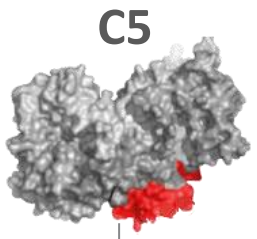
The Terminal Complement Pathway



C5

C5 concentration in blood:
~75 µg/ml (~400 nM)

C5a concentration in blood:
10 ~ 30 ng/ml
(~1-2.5 nM)

C5a

other ligands:
C3a, ASP, C4a etc

C5b

Membrane Attack Complex (MAC)
triggers lysis of pathogens

C5b-9 = MAC

strong amplifier of inflammation

upregulated in many tissues during inflammation

C5aR

C5L2

C5L2 has a different binding pocket for C5a compared to other ligands like C3a, ASP, etc. and this causes different cell signaling.*
The C5a signaling has been shown to be pro-inflammatory.**

other signalling involved e.g. in triglyceride synthesis, etc.

- cell activation
- cytokine generation
- PKC-signaling
- **HMGB-1 induction*** (Inflammasome)

INFLAMMATION

* Kalant D. et. al. J. Biol. Chem. 2003, 278 (13) 11123–11129
**Rittirsch et al. Nat Med. 2008 May ; 14(5): 551; Colley et al. MABS. 2018,10 (1), 104Songlin et. al. J. Biol. Chem. 2019; 294(21) 8384–839 Muenstermann et al.. Virulence, 2020; 10(1) 677-694

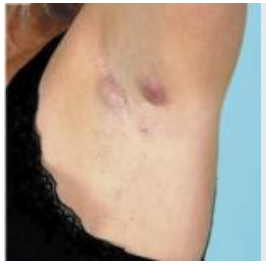
Vilobelimab Immunodermatology Focus

- Hidradenitis Suppurativa (HS)
- Pyoderma Gangraenosum (PG)

Hidradenitis Suppurativa (HS)

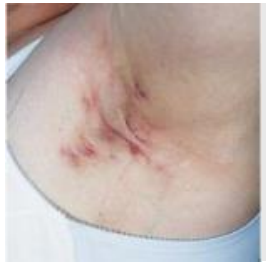
Debilitating C5a-driven inflammatory skin condition with high unmet need

HURLEY STAGING FOR HS



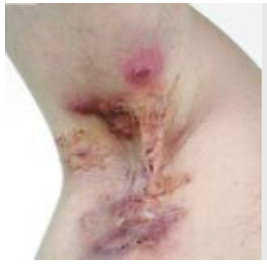
Stage I

Single / multiple abscesses but no sinus tracts or scarring



Stage II

Single or multiple separated, recurrent abscesses with tract formation and scarring



Stage III

Multiple interconnected tracts and abscesses involving an entire anatomic region

Clinical Features

- Chronic, inflammatory, recurrent, debilitating skin disease of the hair follicles
- Most commonly in the armpit, groin and genital regions
- Extremely painful inflammatory nodules, boils or abscesses
- Draining tunnels leading to considerable scarring and functional disability
- Hurley staging system used to classify progression / chronicity (Stage I – III)

Prevalence

- Likely > 200,000 moderate to severe (Hurley II+III) HS patients in US
- Higher prevalence in Europe with reports > 1% total HS prevalence

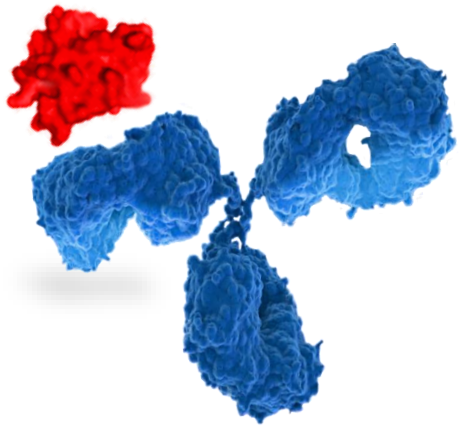
Current Treatment – Medical Need

- Humira®(adalimumab) (TNF-alpha inhibitor) is the only approved biological in US and Europe
- Established (but not approved) standard of care (SOC) includes topical, oral or i.v. antibiotics; in some instances, surgery is required
- Approximately 50% of patients with moderate to severe HS do not respond and about 50% of responder patients lose response to Humira*
- No treatment approved for or targeted at reducing draining tunnels as most burdensome lesion

* Combined Phase III trial data for Humira: response measured by HiSCR 50 and KOL quotes in Sam Slutsky's LifeSci Capital InflaRx initiation report 12/2018

SHINE Phase II Study

Results and Conclusions



RESULTS

- HiSCR primary endpoint and dose response signal not met but signal towards improved AN count for the highest dose cohort
- Statistically significant change in draining tunnels (dTs) and in ANdT count detected for the highest dose cohort
- **Pharmacodynamic studies suggests that higher doses are needed for optimized efficacy**
- Open label extension (OLE): in the responder group, 71% maintain HiSCR response by week 40; signals of sustainable reduction of lesion counts during long term treatment detected (with sub-optimal long-term dosing)

OUR CONCLUSIONS

- **HiSCR is burdened by high variability** (driven by AN count variability) and does not capture reduction of dTs
- **Increased dose required** for full vilobelimab efficacy
- **Reduction in all inflammatory lesions achieved with vilobelimab high-dose** with a durable long-term effect detected even at sub-optimal doses
- **Long-term vilobelimab treatment was well tolerated**, no drug-related serious adverse events (SAEs) in OLE phase

ANdT count = Total number of combined inflammatory nodules, abscesses and draining tunnels
AN count = Total number of combined inflammatory nodules and abscesses

HS Phase III Development

Study Initiation

FDA MEETINGS & NEXT STEPS

FDA Type A meeting (August 2021)

- Received feedback from FDA **supportive of a new primary endpoint measuring reductions in all three inflammatory HS lesions,** including **Draining Tunnels**
  - FDA had previously agreed to the Phase III dosing regimen, a higher dose than studied in the Phase IIB SHINE study
- Pivotal development program to focus on patients suffering from **moderate to severe HS with active draining disease**, as supported by FDA
- FDA feedback incorporated in pivotal study protocol and **submitted in Q4 2021;** The FDA had no comments during the 30-day review period

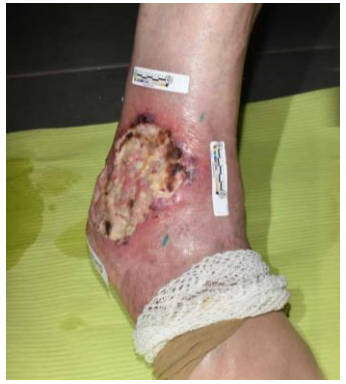
InflaRx has initiated the Phase III with a new primary endpoint, the modified HiSCR

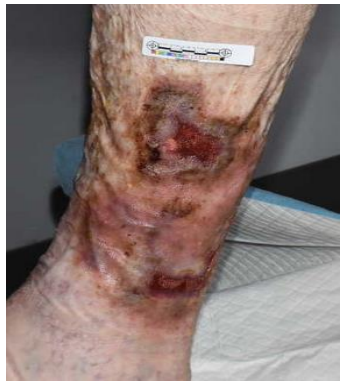
- Details about the new endpoint and the Phase III study design to be shared at virtual R&D event on February 3

InflaRx has initiated the Phase III with a new primary endpoint, the modified HiSCR

Pyoderma Gangraenosum (PG)

AN AUTOIMMUNE CONDITION WITH HIGH UNMET NEED





Clinical Features

- PG is a rare but potentially life-threatening skin disorder that can lead to chronic, highly painful and difficult-to-treat wounds
- Many PG patients also suffer from other autoimmune disorders, such as ulcerative colitis, rheumatoid arthritis, and hematological diseases
- Patients suffer from severe pain, long healing times, and frequent relapses

Incidence

- Rare - Estimated that up to 50,000 patients in the US and Europe are affected

Current Treatment – Medical Need

- No drugs currently approved in the US or EU
- For less severe cases, topical or intralesional treatments can be used, including topical steroids
- Use of systemic immunosuppression in rapidly progressing cases
- Mixed reports about efficacy, long treatment durations, relapses are frequently seen

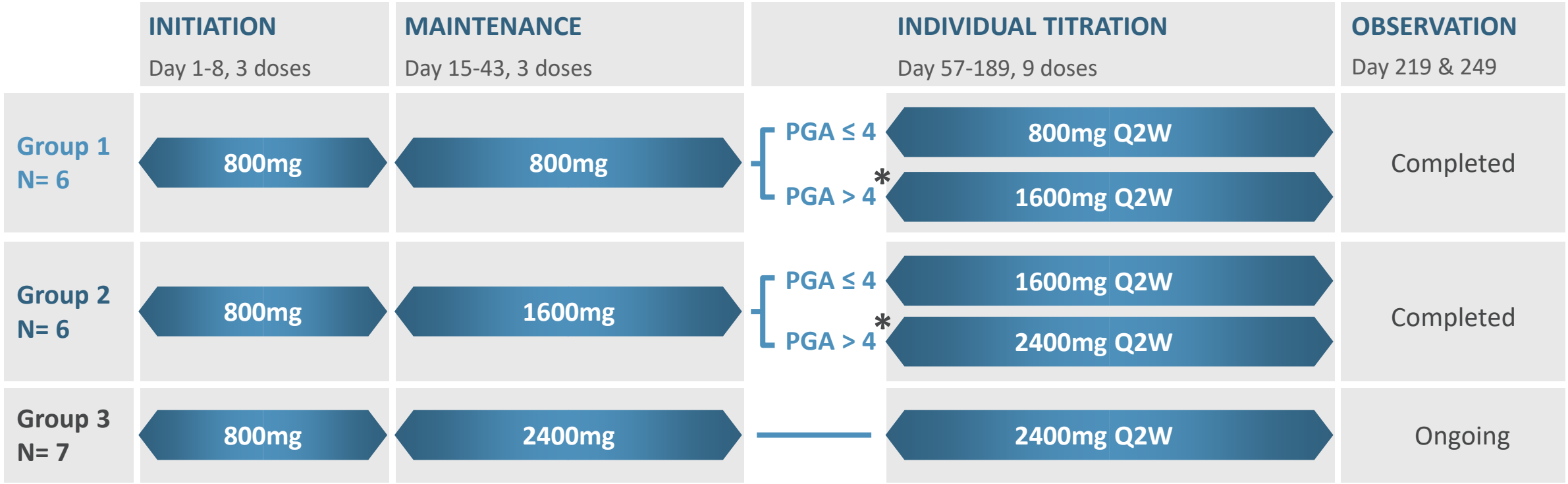
Strong rationale for treatment with vilobelimab: PG associated with neutrophilic skin infiltration in affected areas and lesions, potentially triggered by C5a

Photo Source: InflaRx study

PG Phase IIa

Study Design

- 19 patients enrolled in the study
- **Primary endpoint:** Safety
- **Key secondary endpoints:** Responder rate defined as PGA ≤3 (PGA of ≤1 is considered clinical remission and closure of target ulcer); Time to complete closure of target ulcer



* Uptitration to the next dose on day 57 **if** PGA > 4 and at least 5 patients treated with the current dose showed no safety issues

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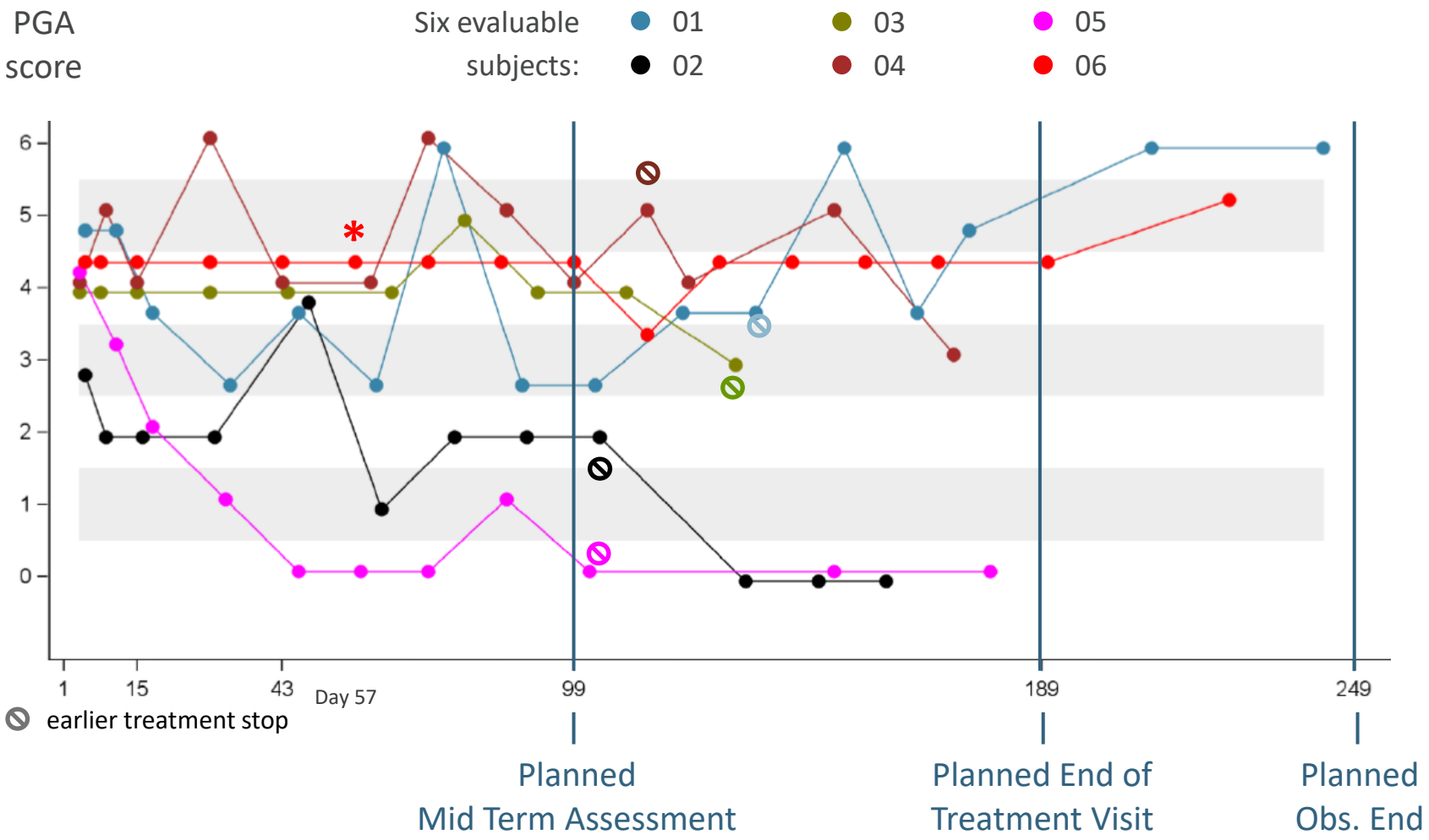
Study Results – Group 1 (Low Dose)

PGA-line plot of absolute values over time by patient *(Actual days displayed acc. to visit windows)*



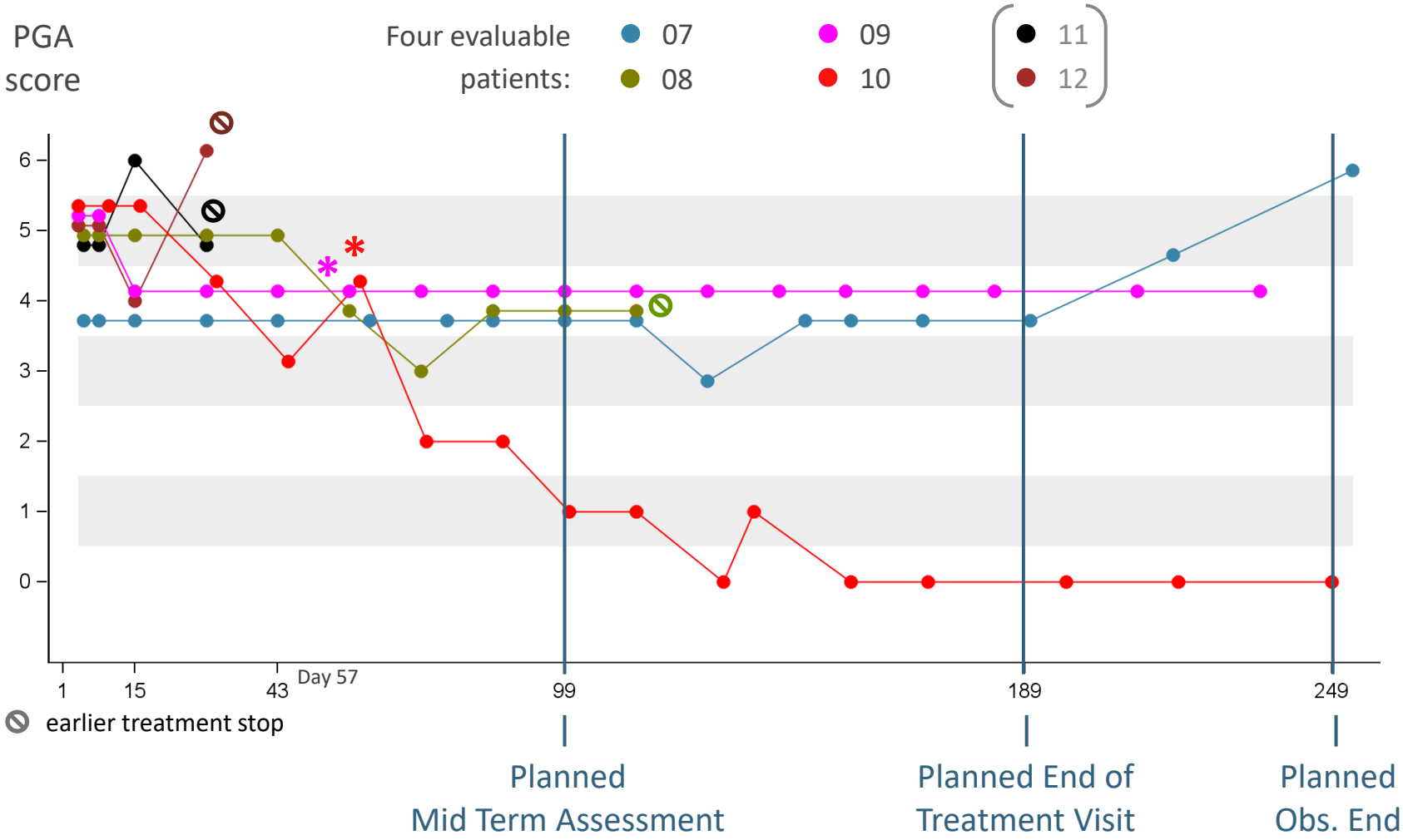
GROUP 1 RESULTS

- Two patients (02 and 05) achieved **complete remission of target ulcer**
- One patient (01) with initial response and fluctuating PGA
- Patients 02 and 05 stopped treatment before Day 189 based on investigator decision because of complete disease remission
- Patient 03 dosed until Day 130 but stopped treatment due to Covid situation. No follow up.

* Uptitration to 1600mg on day 57 **if** PGA > 4 and at least 5 patients treated with 800mg show no safety issues. Applied to patient 06

Study Results – Group 2 (Medium Dose)

PGA-line plot of absolute values over time by patient *(Actual days displayed acc. to visit windows)*



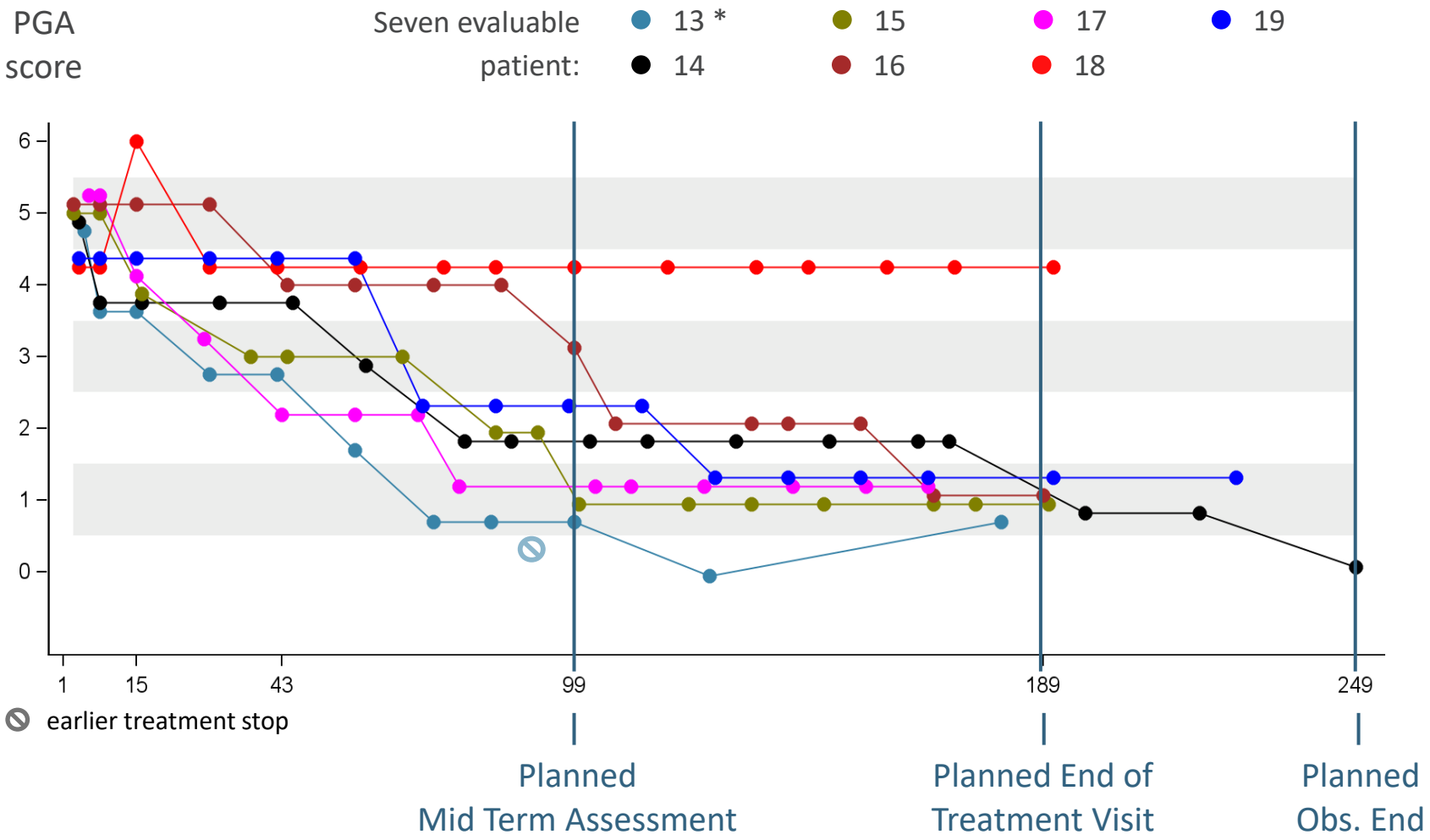
GROUP 2 RESULTS

- One patient (10) out of four **healed upon up-titration to 2400mg group on day 57** with PGA = 0 since visit 12 (closure of large target ulcer area)
- Two patients (08, 09) showed temporary response, not considered responder
- Two patients (11, 12) discontinued early in study and were non-evaluable

* Uptitration to 2400mg on day 57 **if** PGA > 4 and at least 5 patients treated with 1600mg show no safety issues. Applied to patients 09 and 10

Study Results – Group 3 (High Dose)

PGA-line plot of absolute values over time by patient *(Actual days displayed acc. to visit windows)*



* Patient 13 was discontinued from treatment after day 71 due to delayed availability of pos. baseline TB testing result (exclusion criterion). No re-activation of TB reported up to end of observation.

GROUP 3 RESULTS

- Six patients out of 7 achieved PGA score of ≤ 1 (remission)
- One patient (18) experienced target ulcer area decrease >50%; however, new PG lesions developed
- Patient 19 with complicated disease course
  - Pre-existing diabetes and wound infection in target ulcer area on day 1 with start of antibiotics
  - Wound infection and local progression in target ulcer area on day 50
  - Broad spectrum antibiotics and cyclosporin A starting day 50
  - Closure of target ulcer on day 127
- Patient 16 started 10 mg/d prednisone on day 72 (allowed per protocol)

PG Phase IIa

Patient 10 Case Study

TARGET ULCER REAPPEARED IN AUGUST 2020

MH: PG since Jun 2019, Hypertension since 1998; **Study Day 1:** Feb 2021

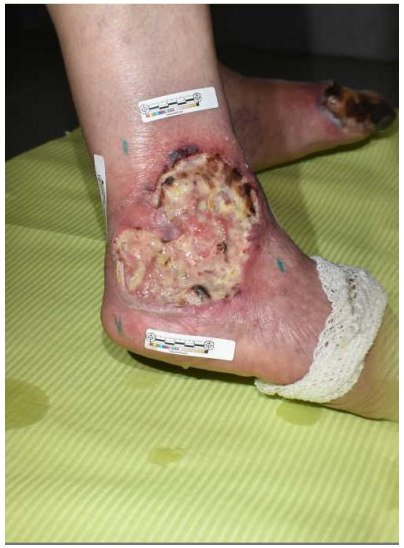
Cohort 2: 1600 mg Q2W, individual uptitration to 2400 mg at D57, treatment completed

Previous PG medication: Methylprednisolone only in Jun 2019**,** Dapsone Jun 2019- Aug 2020, Cyclosporine Oct 2019- Aug 2020 -> ulcer healed and reappeared soon after discontinuation of immunosuppressants

Concomitant Medication: Prednisone 10 mg for PG since October 2020

Baseline

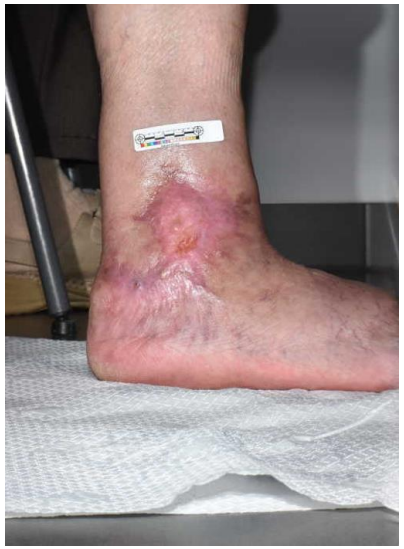
Area: 3695 mm^2



Day 99

PGA = 1

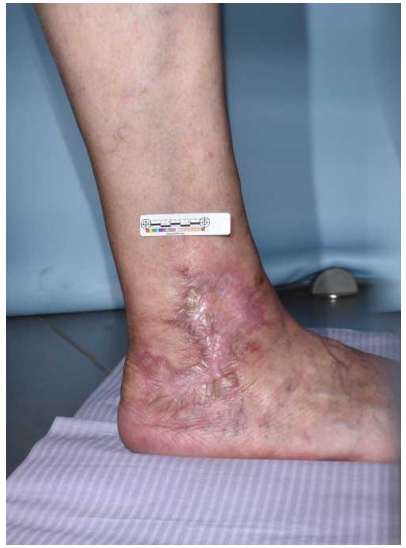
Area: 0.00 mm^2



Day 189, V16 (20 days after last vilo. admin.)

PGA = 1

Area: 0.00 mm^2



PG Phase IIa

Patient 14 Case Study

PG TREATMENT HISTORY: CICLOSPORIN, DAPSONE

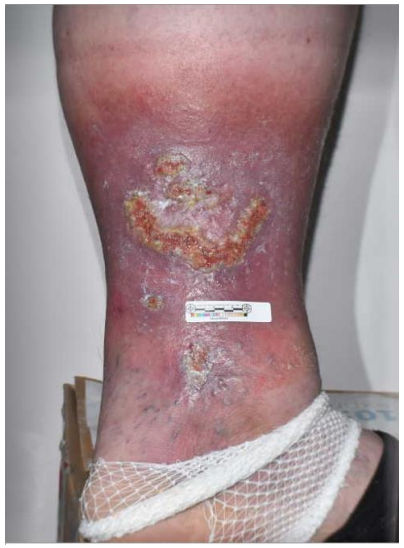
MH: PG since October 2018, Obesity since longer time (no exact day available)
Treatment Start: February 2021

Cohort 3: 2400 mg Q2W treatment completed
Previous PG medication: Ciclosporin and methylprednisolone October 2018 – September 2019, failed. Dapsone September 2020 – November 2020.

Concomitant Medication: Prednisone 10 mg since October 2018

Baseline

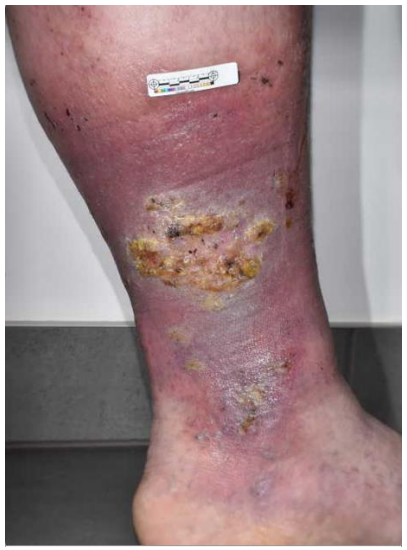
Area: 1285 mm^2



Day 99

PGA = 2

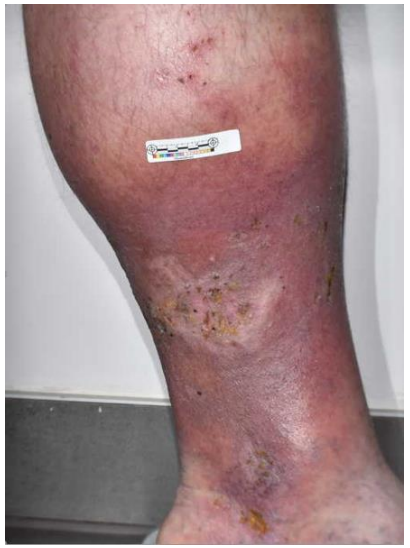
Area: 0.0 mm^2



Day 189, V16 (20 days after last IFX-1 admin.)

PGA = 1

Area: calculation not yet available



PG Phase IIa

Patient 13 Case Study

TARGET ULCER OPENED IN NOVEMBER 2020 WHILE ON STABLE ADALIMUMAB

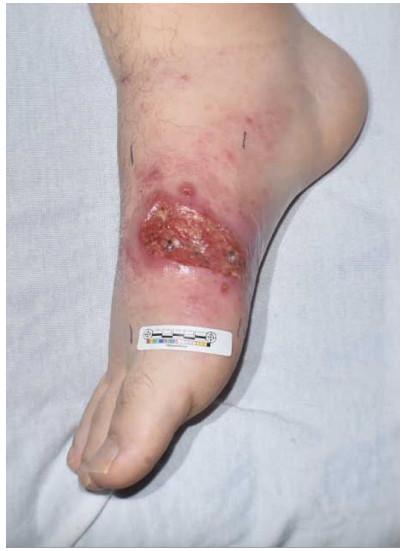
MH: PG since August 2020, Psoriasis since 2017
Treatment Start: March 2021
Previous PG medication: None

Cohort 3: 2400 mg Q2W up to Day 85 → exclusion after 9 doses due to delayed availability of pos. baseline TB testing result (no TB activation!)

Concomitant Medication: Adalimumab for psoriasis 40 mg QD since 2017

Baseline

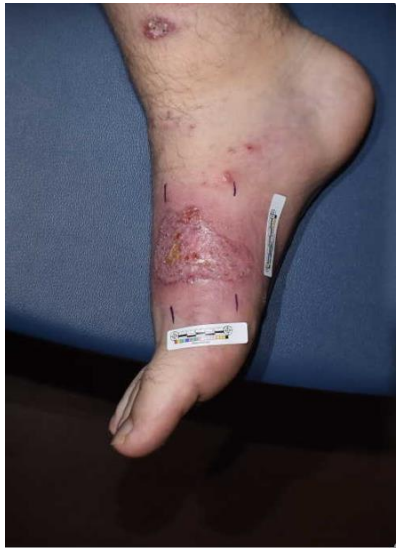
Area: 1136 mm^2



Day 85

PGA = 1

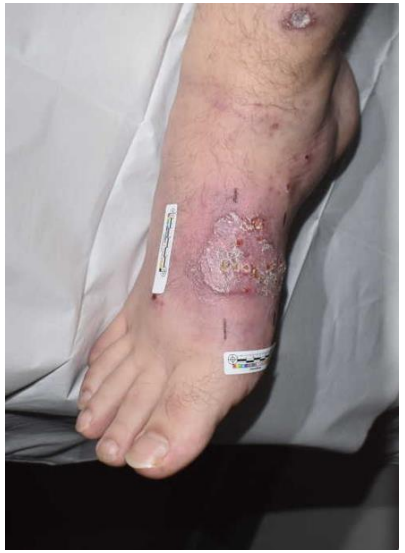
Area: 0.00 mm^2



Day 89, end of treatment visit

PGA = 1

Area: calculation not yet available



PG Phase IIa Study Results

Summary and Conclusion

SAFETY CONCLUSION

- No infusion-related reactions observed
- For 2 patients, related SAEs were reported:
  - Erysipelas leading to hospitalization (judged as non-related by sponsor)
  - Rash due to delayed hypersensitivity reaction
- Observed AE profile in line with patients' underlying diseases
- No dose-related AEs detected

CLINICAL RESPONSE CONCLUSION

- Out of 17 evaluable patients at end of treatment visit or day of last drug administration
  - Clinical Remission (PGA ≤ 1): 9 patients (53%)
  - Clinical Response (PGA ≤ 3): 1 additional patient (6%)
  - Slight Improvement (PGA = 4): 7 patients (41%)
- **High dose group shows highest rate of target ulcer closure and clinical remission (85.7%)**

WE WILL MEET WITH FDA TO DISCUSS NEXT STEPS

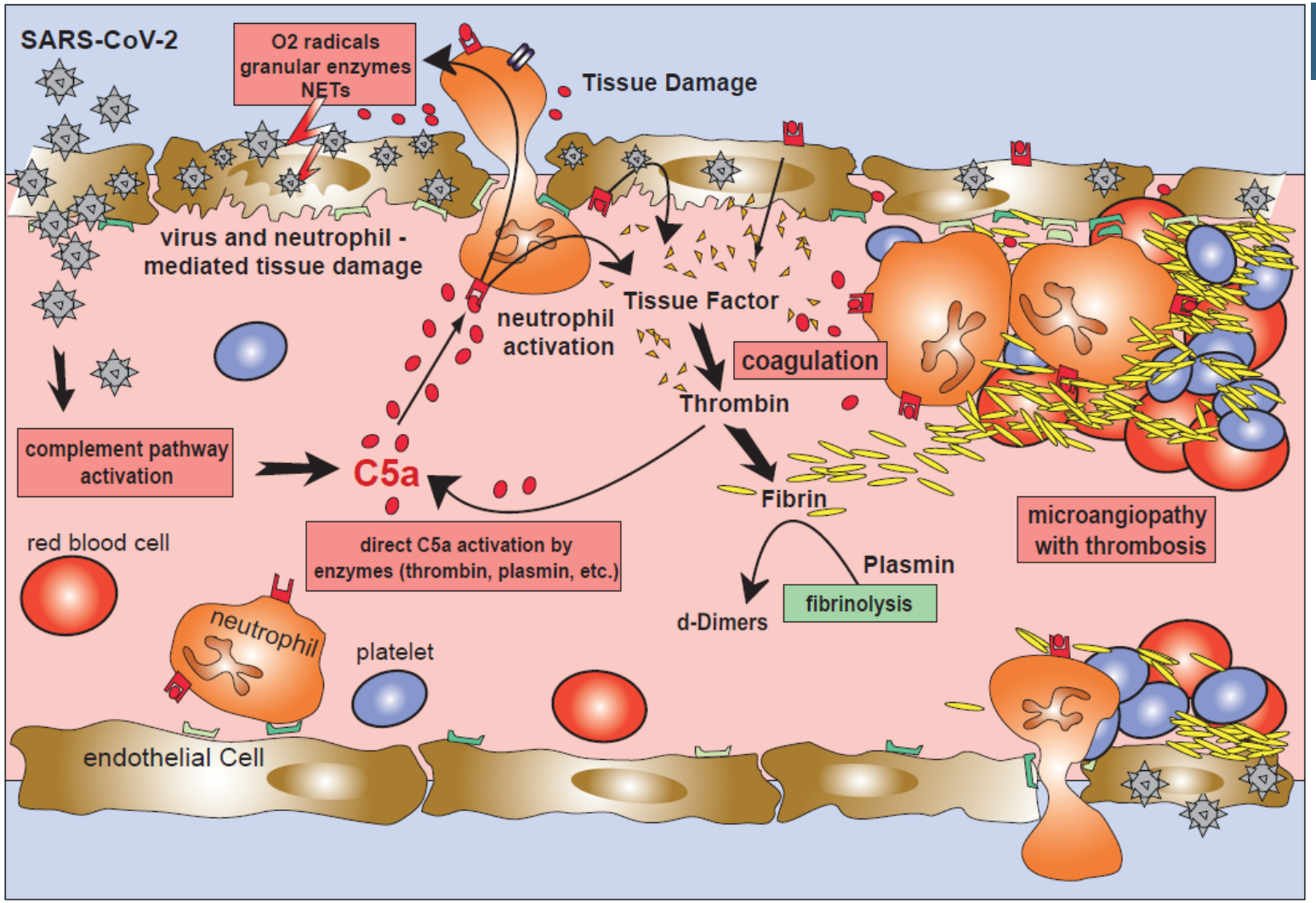
Vilobelimab Q2W shows good safety and tolerability
Evidence of dose-dependent drug activity in PG

Vilobelimab
Life-threatening Inflammatory Diseases

- COVID-19
- ANCA Associated Vasculitis (AAV)

COVID-19 induced Vascular Injury – Potential Role of C5a

Model for Proposed Mode of Action of C5a in COVID-19 induced vascular injury



Source: InflaRx GmbH

OUR HYPOTHESIS

- Endothelial damage is induced by SARS-CoV-2 infection which also activates the complement system leading to C5a generation.
- C5a activates neutrophils via C5aR, leading to increased adherence to endothelial cells and damage through generation of oxidative radicals, granular enzyme release and neutrophil extracellular traps (NETs).
- C5a induces release of tissue factor from neutrophils & endothelial cells, which promotes coagulation, leading to Fibrin formation.
- Thrombin, plasmin and other enzymes can further induce direct C5a activation (through direct cleavage of C5), which may establish a viscous circle leading to microangiopathy with thrombosis

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Phase II Part Results

Overview

PHASE II STUDY RESULTS*

Primary endpoint:

- No difference detected in improvements between groups in PaO2/FiO2 ratio
- High variability between patients
- Conclusion: Endpoint not suitable as response parameter

Key secondary and other endpoints - Observed effects with vilobelimab compared to best standard of care:

- **50% lower all-cause mortality rate** (13% in vilobelimab group vs 27% for control group)
- **Fewer patients experienced renal impairment** assessed by estimated glomerular filtration rates
- **Faster reversal of blood lymphocytopenia**
- **Reduction in tissue damage**: Greater lowering of lactate dehydrogenase concentrations
- Temporary but **statistically significant increase in D-dimer levels** in first days after vilobelimab administration - **potential signal of induction of blood clot lysis**

* Vlaar, A et al. *Lancet Rheumatol 2020*. https://doi.org/10.1016/S2665-9913(20)30341-6

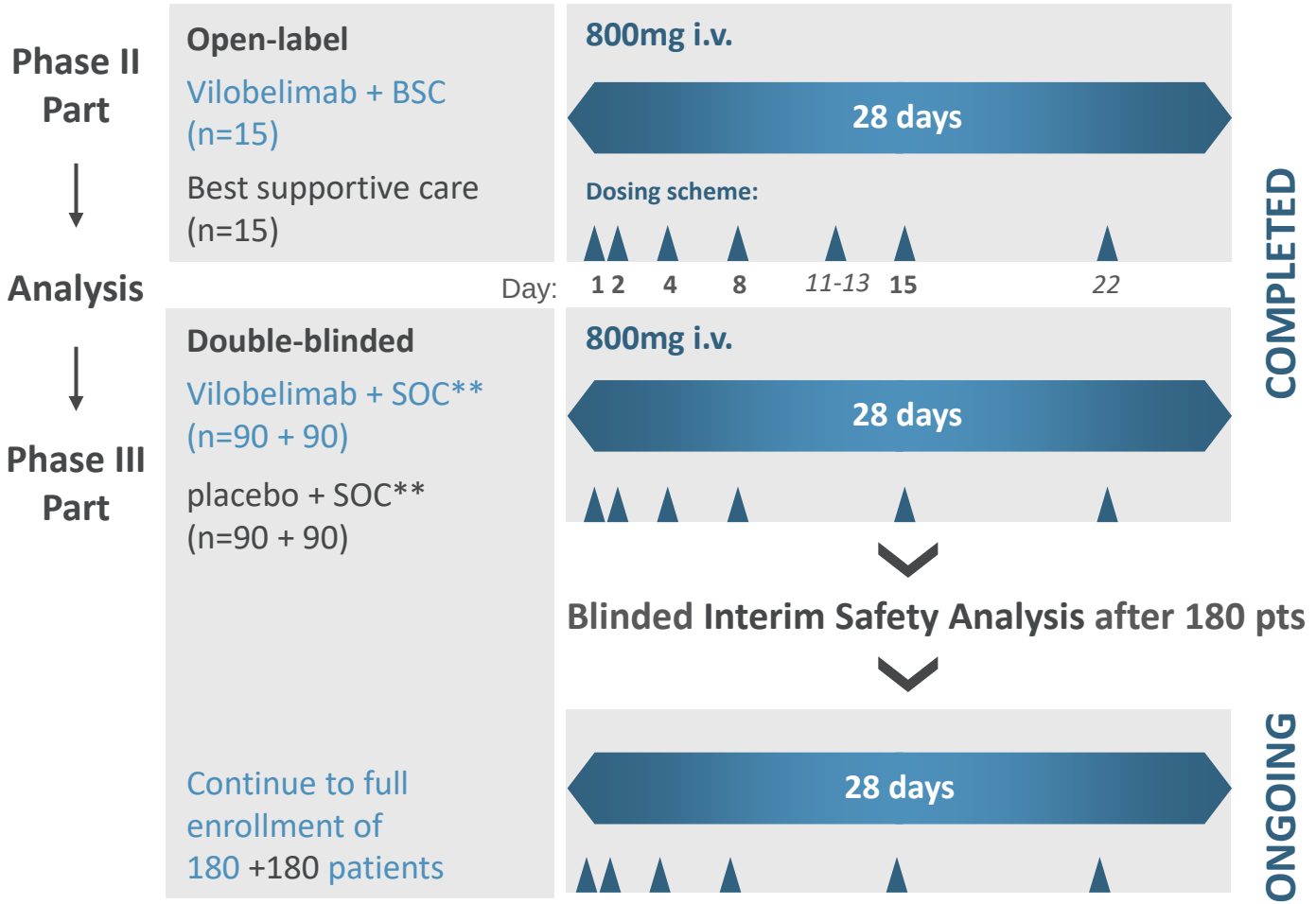
Design of Phase II/III Study with Vilobelimab in Severe COVID-19

STUDY DESIGN

- Critically ill intubated* patients with COVID-19 induced pneumonia
- Phase III primary endpoint: 28-day all-cause mortality
- Other key endpoints include assessments of organ support, disease improvement on ordinal scale

STATUS

- **Phase II part completed:**
  Topline results published
- **Phase III part fully enrolled: *369 patients***
  Topline data expected by Q1 2022
- IDMC recommended continuing the trial at interim analysis (180 patients evaluated)



* In Phase III part, eligible patients must be early intubated. In the Phase II part, patients were enrolled if either early intubated or dependent on oxygen delivery

** SOC includes venous thromboembolism prophylaxis at a minimum and may include other specific recommended treatments for COVID-19 per the locally adopted treatment recommendation

Phase II Studies in AAV

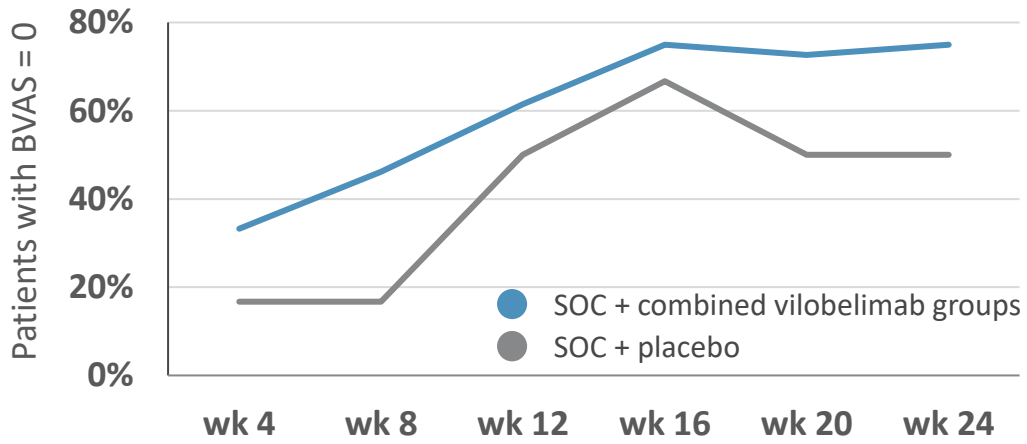
Results

EU PHASE II TOPLINE RESULTS (N=57 TOTAL)

- Demonstrated **Proof of concept** for vilobelimab to reduce use of **glucocorticoid (**GC) therapy in AAV
- Achieved comparable efficacy to standard of care GC therapy
- Use of vilobelimab instead of GC led to a **substantially lower observed glucocorticoid toxicity**
- Lowest vasculitis damage index (VDI) total score at week 16 in vilobelimab only group

US PHASE II TOPLINE RESULTS (N=19)

- **Primary endpoint met; safe and well-tolerated** in patients with AAV
  Observed TEAEs are reflective of the disease and SOC treatment
- All three treatment groups showed **a strong clinical response** (50% reduction in BVAS) **at week 16**
- **Clinical remission** (BVAS = 0): **higher number & percentage of patients in remission in vilobelimab groups at various timepoints**



TEAEs: Treatment-emergent adverse events

inflaRx

Vilobelimab
Oncology

- Cutaneous Squamous Cell Carcinoma (cSCC)

Cutaneous Squamous Cell Carcinoma (cSCC)

Phase II Study Underway

POTENTIAL ROLE OF C5A IN ONCOLOGY & cSCC

- **C5a induces an immunosuppressive tumor microenvironment**
- **C5a promotes metastases**
- **C5a is readily available in the tumor environment and may promote tumor growth directly**

PRIMARY ENDPOINTS

- Arm A: Assess antitumor activity of vilobelimab
- Arm B: Determine maximum tolerated dose (MTD) or recommended Phase II dose (RP2D); Assess antitumor activity and safety profile of vilobelimab + pembrolizumab

DISEASE INFORMATION cSCC

- **Estimated incidence: 15-35 per 100,000 people**; expected to increase 2-4% per year; **Metastasizes in approximately 2-5%** of cases[1,2,4]
- Advanced SCC 10-year survival rates <**20%** with regional lymph node involvement and **<10%** with distant metastases; Distant metastases have median survival of <2 years[1,3]
- PD-1 checkpoint inhibitors pembrolizumab or cemiplimab are FDA approved for locally advanced, recurrent or metastatic cSCC (see FDA labeling)
- No treatment is available for PD-1 or PD-L1 resistant or refractory patients

› Inhibition of C5a signaling in the tumor microenvironment may decrease tumor growth
Combination of C5a with PD-1 checkpoint inhibition could reverse resistance to PD-1 or PD-L1 inhibitor therapy

1. Stratigos et al., 2015; 2. Burton et al., 2016; 3. Hillen et al., 2018; 4. Li et al, 2015

INF904
New Pipeline Program

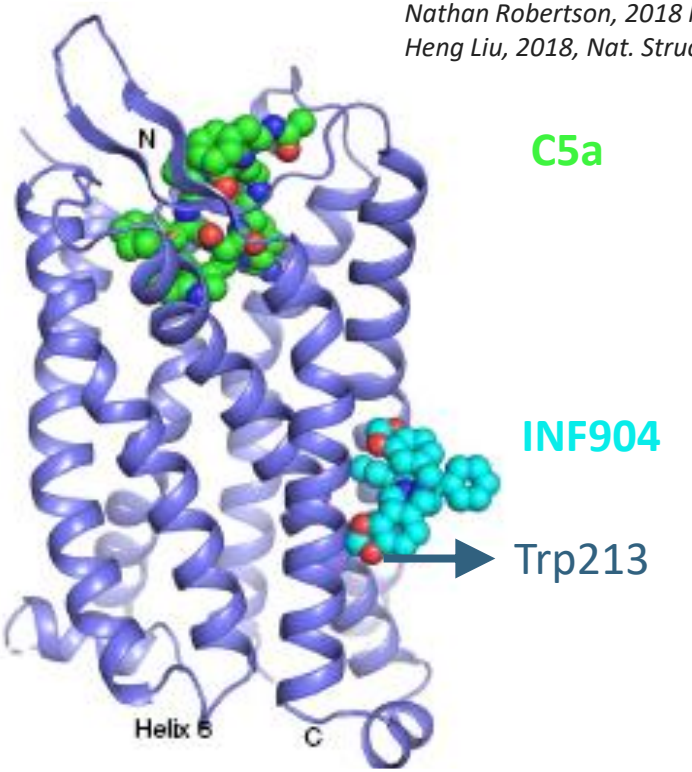
Background

C5aR and its allosteric inhibitor INF904

C5a and INF904

- **C5a receptor (C5aR):**
  - a 7-transmembrane G-protein-coupled-receptor expressed primarily on granulocytes, mediates the major pathophysiological effects of C5a
  - C5aR proven to be an important drug target with FDA approval of a chemical C5aR inhibitor in AAV in 2021
- **INF904 binds to a well-known allosteric site in C5aR**
- **INF904 has a novel Markush structure**
- **US patent was issued in October 2021**

Nathan Robertson, 2018 Nature
Heng Liu, 2018, Nat. Struct. Mol. Biol



C5a binds to orthosteric binding site on the top
INF904 bind to allosteric binding site on the side

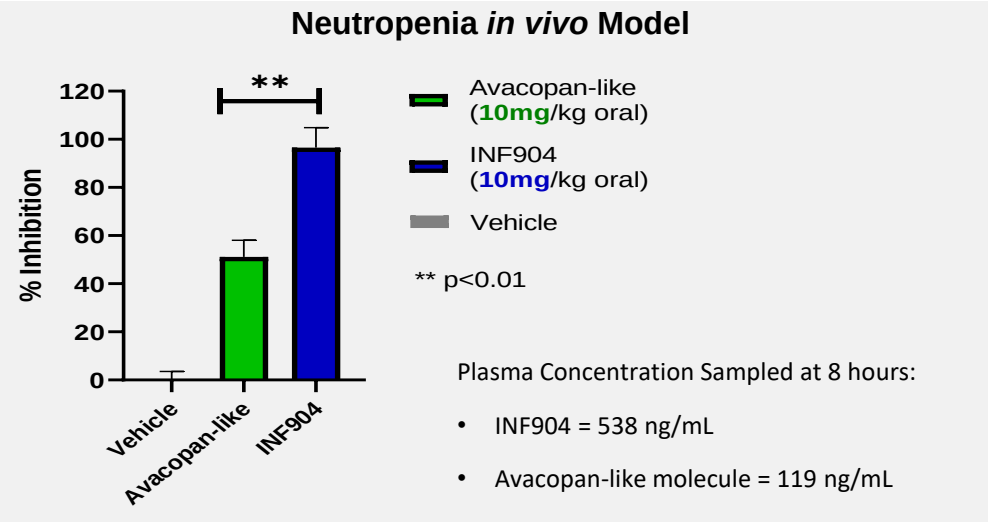
inflaRx

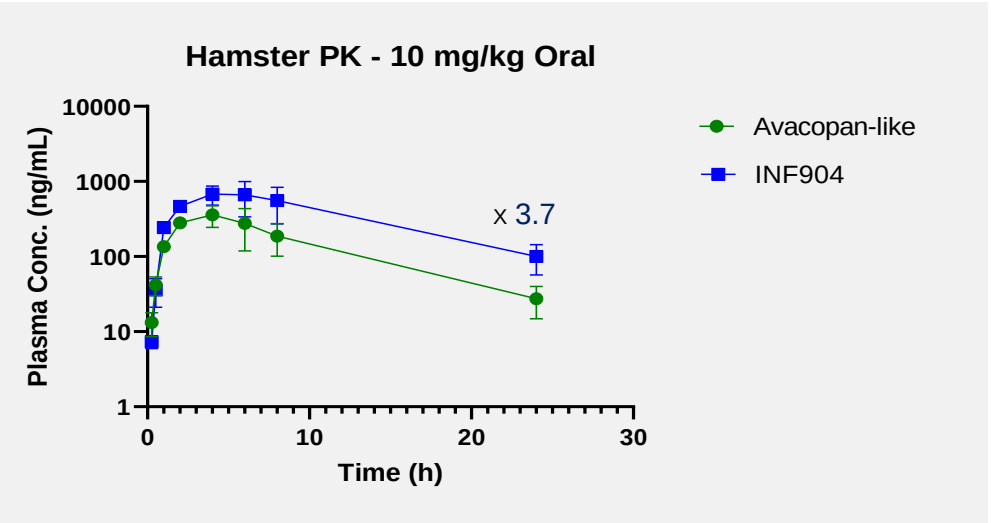
INF904

Potential for Best in Class C5aR Inhibition

PROGRAM DETAILS

- INF904 shows **no obvious toxicological findings** even in the highest dose groups in required GLP toxicity analyses
- INF904 shows a **high in vitro potency** with a desired IC50 (<1nM) in calcium mobilization assay
- In vitro analysis of INF904's effect on CYP3A against Avacopan-like molecule shows **significantly less CYP3A4/5 inhibition** which play an important role of metabolic clearance of glucocorticoids
- Oral INF904 shows **higher plasma exposures** in several in-vivo models vs. Avacopan-like molecule
- Oral INF904 shows a **better potency in in-vivo neutropenia model** vs. Avacopan-like molecule
- Oral INF904 shows **therapeutic benefit / efficacy** in renal disease models and peritonitis model
- **Regulatory discussions on Phase I program have been initiated**
- **First-in-human clinical trial expected to start in H2 2022**





Strategy and Outlook

Strategic Objectives

Immuno-dermatology Focus

- **HS: Initiate Phase III program** with vilobelimab, incorporating novel endpoint
- **PG:** Advance vilobelimab **towards Phase III based on regulatory guidance**

Additional Potential Upside

- **Severe COVID-19: Complete Phase III** with vilobelimab; **Submit for approval** if results are positive
- **AAV:** Discuss next steps for vilobelimab with regulatory authorities
- **Oncology:** Continue to explore clinical application of vilobelimab
- **Advance INF904 into first-in-human study**

Strong cash balance to pursue these activities: €120.6 million as of September 30, 2021

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