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# PRIME Phase 1b Top-line Data Review

NASDAQ: REVB

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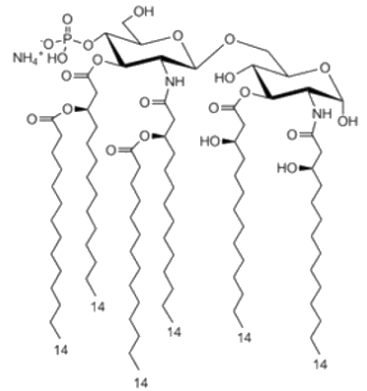
# Forward-Looking Statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These forward-looking statements are generally identified by the words "anticipate", "believe", "expect", "estimate", "plan", "outlook", and "project" and other similar expressions. We caution investors that forward-looking statements are based on management's expectations and are only predictions or statements of current expectations and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from those anticipated by the forward-looking statements. Revelation cautions investors not to place undue reliance on any such forward-looking statements, which speak only as of the date they were made.

The following factors, among others, could cause actual results to differ materially from those described in these forward-looking statements: the ability of Revelation to meet its financial and strategic goals, due to, among other things, competition; the ability of Revelation to grow and manage growth profitability and retain its key employees; the possibility that the Revelation may be adversely affected by other economic, business, and/or competitive factors; risks relating to the successful development of Revelation's product candidates; the risk that our preclinical studies will not demonstrate sufficient positive data to support commencement of clinical trials; the risk that we may not fully enroll our clinical studies or enrollment will take longer than expected; risks relating to the occurrence of adverse safety events and/or unexpected concerns that may arise from data or analysis from our clinical studies; changes in applicable laws or regulations; expected initiation of the clinical studies, the timing of clinical data; the outcome of the clinical data, including whether the results of such study is positive or whether it can be replicated; the outcome of data collected, including whether the results of such data and/or correlation can be replicated; the timing, costs, conduct and outcome of our other clinical studies; the anticipated treatment of future clinical data by the FDA, the EMA or other regulatory authorities, including whether such data will be sufficient for approval; the success of future development activities for Gemini or any other product candidates; potential indications for which product candidates may be developed; the ability of Revelation to maintain the listing of its securities on NASDAQ; the expected duration over which Revelation's balances will fund its operations; the ability of Revelation to obtain further financing and other risks and uncertainties described herein, as well as those risks and uncertainties discussed from time to time in other reports and other public filings with the SEC by Revelation.

# Gemini™ Platform

The Gemini[1] platform is based on the API PHAD®



| Program | Therapeutic Indication | Discovery | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|---|---|
| GEM-AKI | Acute Kidney Injury | | | | |
| GEM-CKD | Chronic Kidney Disease | | | | |
| GEM-PSI | Post Surgical Infection | | | | |
| GEM-PBI | Post Burn Infection | | | | |
| Portfolio | Multiple[2] | | | | |

[1] Gemini is our proprietary formulation platform intended to optimize PHAD's route of administration appropriate for a specific condition

[2] Initially focused on acute indications to leverage existing IND and acute clinical data

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# Key Study Findings

- Primary safety endpoint met – no serious or severe adverse events up to target dose
- Gemini significantly reduced background inflammation to normal levels and restored normal cell response to stimuli in peripheral blood mononuclear cells (PBMCs) demonstrating rebalancing of immune response
- The rebalancing effect was shown to be durable

**Based on these results we believe Gemini has the potential to revolutionize the treatment of ongoing chronic and acute inflammatory conditions**

# PRIME – PRotective IMmunostimulatory Evaluation

## A Phase 1b, Randomized, Placebo Controlled, Single Blind, Single-Ascending Dose in Stage 3 and Stage 4 CKD Patients

### Design

- Single dose, dose escalation
- 5 cohorts, 8 subjects per cohort 1:4 placebo vs drug (up to 40 patients)
  - Cohort 1 – Subtherapeutic dose to evaluate safety in this patient population
  - Cohort 2 – Low dose
  - Cohort 3 and 4 – Target dose
  - Cohort 5 – High dose
- Follow for 7 days
- An extension study to collect 8 additional PBMC/biomarker samples in naïve/secondary naïve patients was also conducted

### Readouts

- Safety, tolerability, PK, and biomarkers of activity
- **Measurement of immune cell (PBMC) response, inflammatory state, and reaction to proinflammatory HMGB-1[1] and LPS[2]**
- Measurement of proinflammatory and anti-inflammatory cytokines

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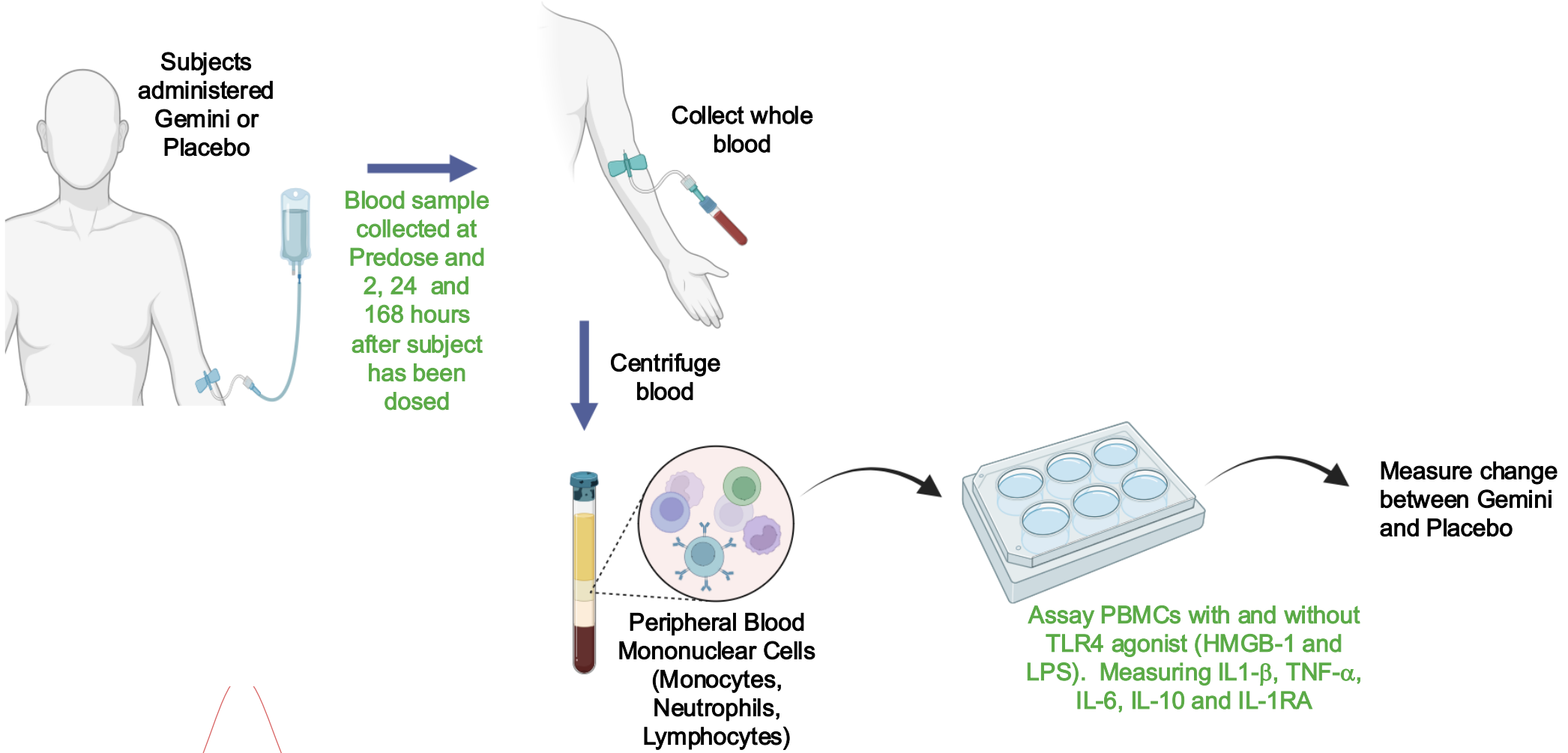
[1]Results foHMGB-1: High mobility box protein-1 is an endogenous damage associated molecular pattern (DAMP) that is generated during tissue injury (e.g. during surgery) which drives the inflammatory response
[2]LPS: Lipopolysaccharide is an exogenous pathogen associated molecular pattern (PAMP) that is generated from a bacterial infection and drives the inflammatory response associated with infection (e.g. fever)

# Peripheral Blood Mononuclear Cell (PBMC) Methodology

Evaluation of PBMCs collected at different time points post-dose provide a picture of the in vivo effect of Gemini at the cellular level over time



# Patients were Divided into Two Groups for Analysis

- Patient PBMCs with a high background of inflammation (IL-1β) at predose: all patients with >10x the limit of quantitation for IL-1β (>40 pg/mL) at predose
  - PBMCs with high background inflammation do not respond to stimulation with LPS or HMGB-1 (immunoparalysis)
- Patient PBMCs with low background inflammation (IL-1β) at predose: all patients with (≤40 pg/mL) at predose
  - PBMCs with low background inflammation do respond to LPS or HMGB-1 stimulation (immunocompetent)
- Distribution of patients in each group by cohort:

| IL-1β Range | Placebo | Low dose[1] | Target dose | High dose[1] | Total |
|---|---|---|---|---|---|
| ≤ 40 pg/mL | 7 | 5 | 6 | 4 | 22 |
| >40 pg/mL | 9 | 3 | 6 | 2 | 20 |

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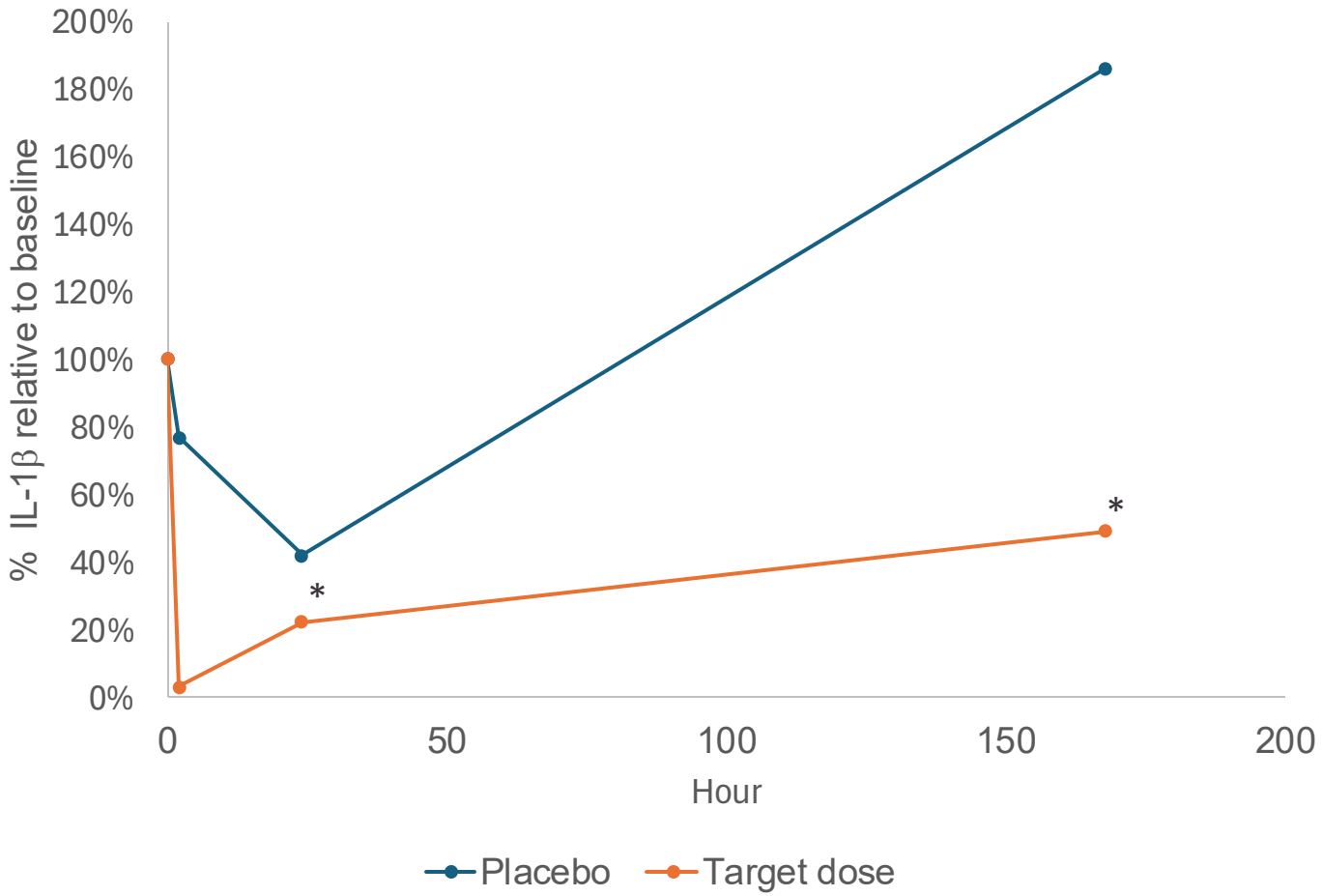
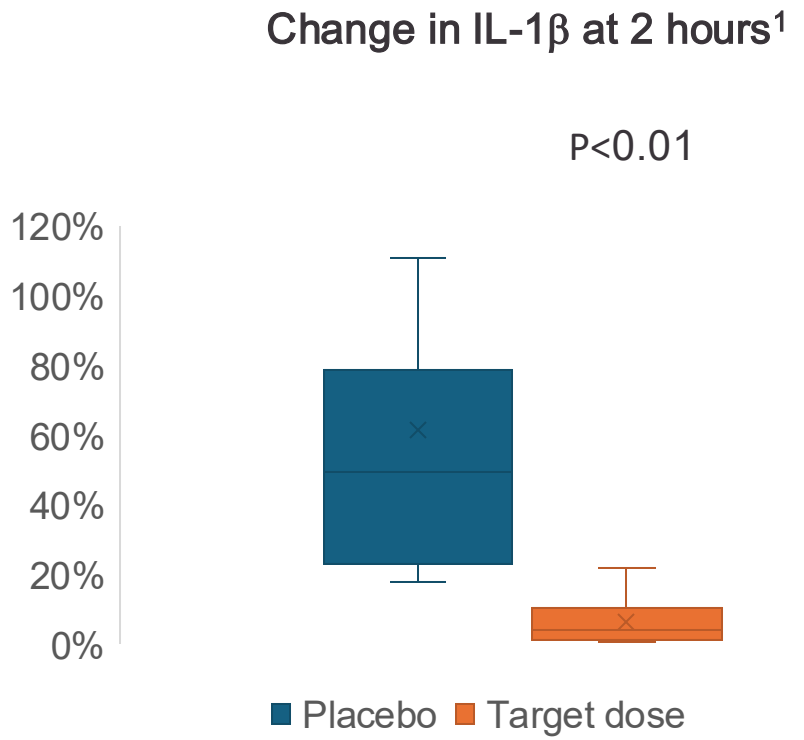
[1]Results for high and low dose groups consistent with those observed for target dose group but are not presented herein

# Effect of Gemini on Patient PBMCs with High Background Inflammation

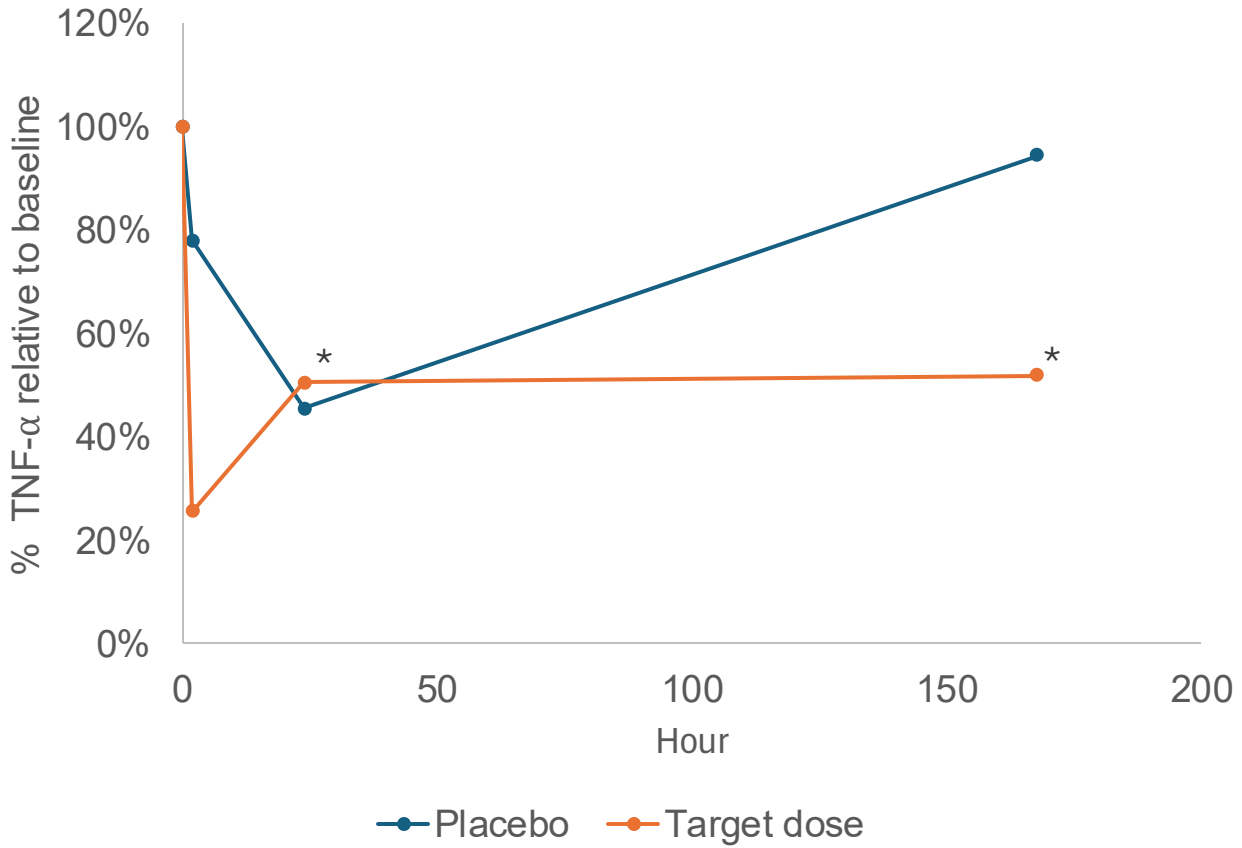
# Gemini significantly reduces IL-1β production compared to placebo

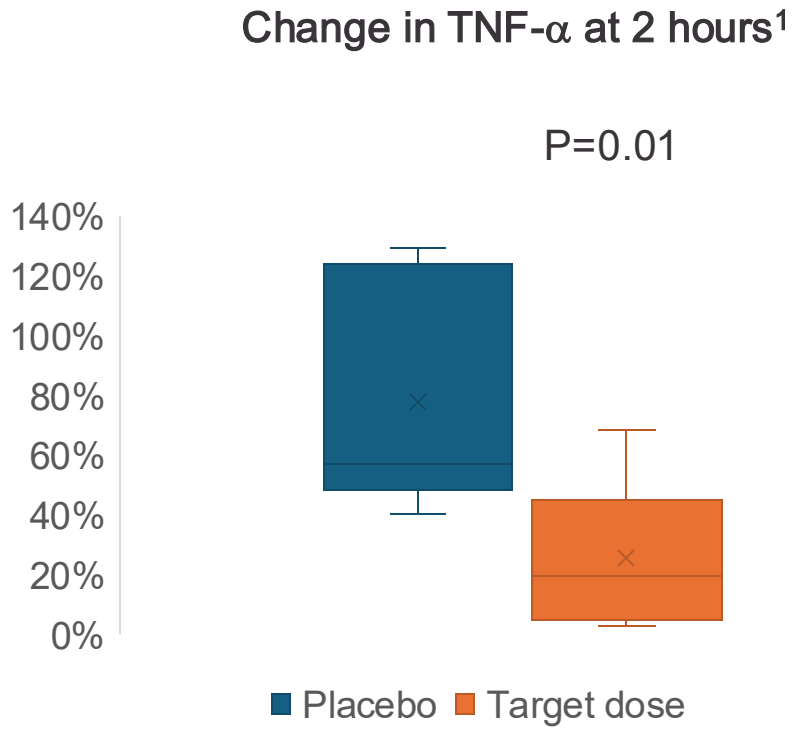



[1]p value based on 2-tailed t-test
*Reduction in IL-1β activity in treated group remains significantly below pre-dose baseline at 24 hours (p<0.001) and trends lower at 168 hours post dose (p 0.07), p values based on 1-tailed t-test

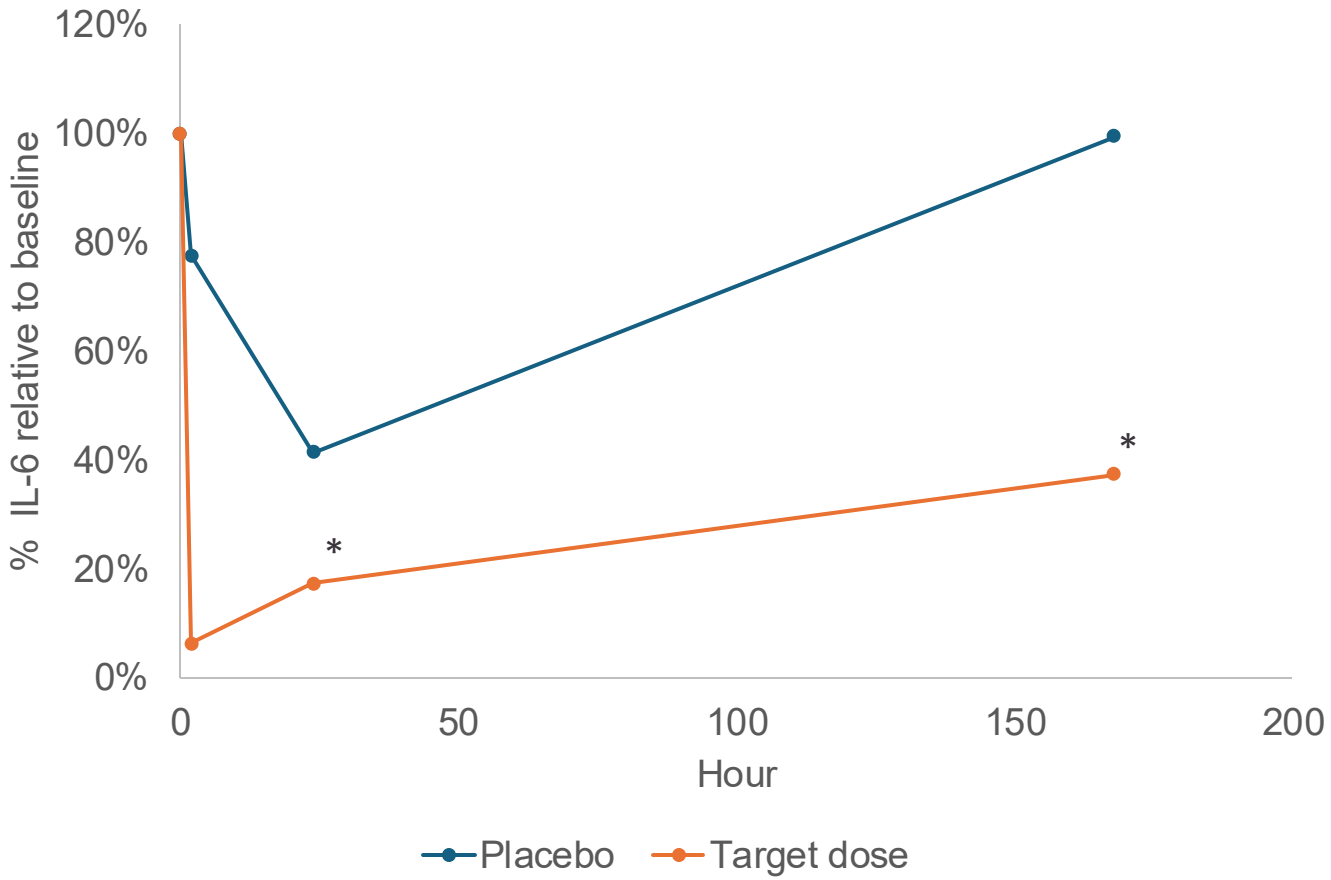
# Gemini significantly reduces TNF-α production compared to placebo

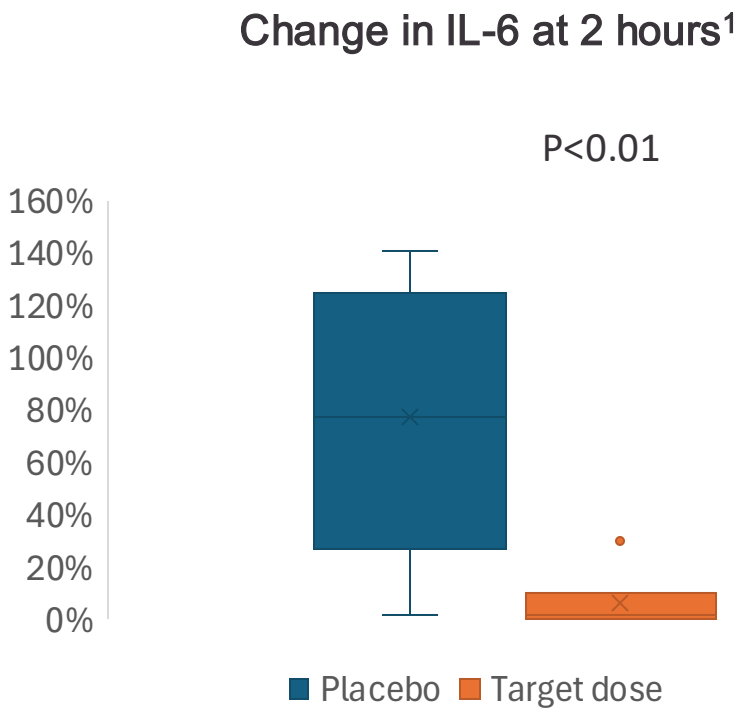



[1]p value based on 2-tailed t-test
*Reduction in TNF-α in treated group remains significantly below pre-dose baseline at 24 hours (p<0.03) and 168 hours post dose (p 0.04), p values based on 1-tailed t-test

# Gemini significantly reduces IL-6 production compared to placebo




[1]p value based on 2-tailed t-test
*Reduction in IL-6 in treated group remains significantly below pre-dose baseline at 24 hours (p<0.0001) and 168 hours post dose (p <0.02), p values based on 1-tailed t-test

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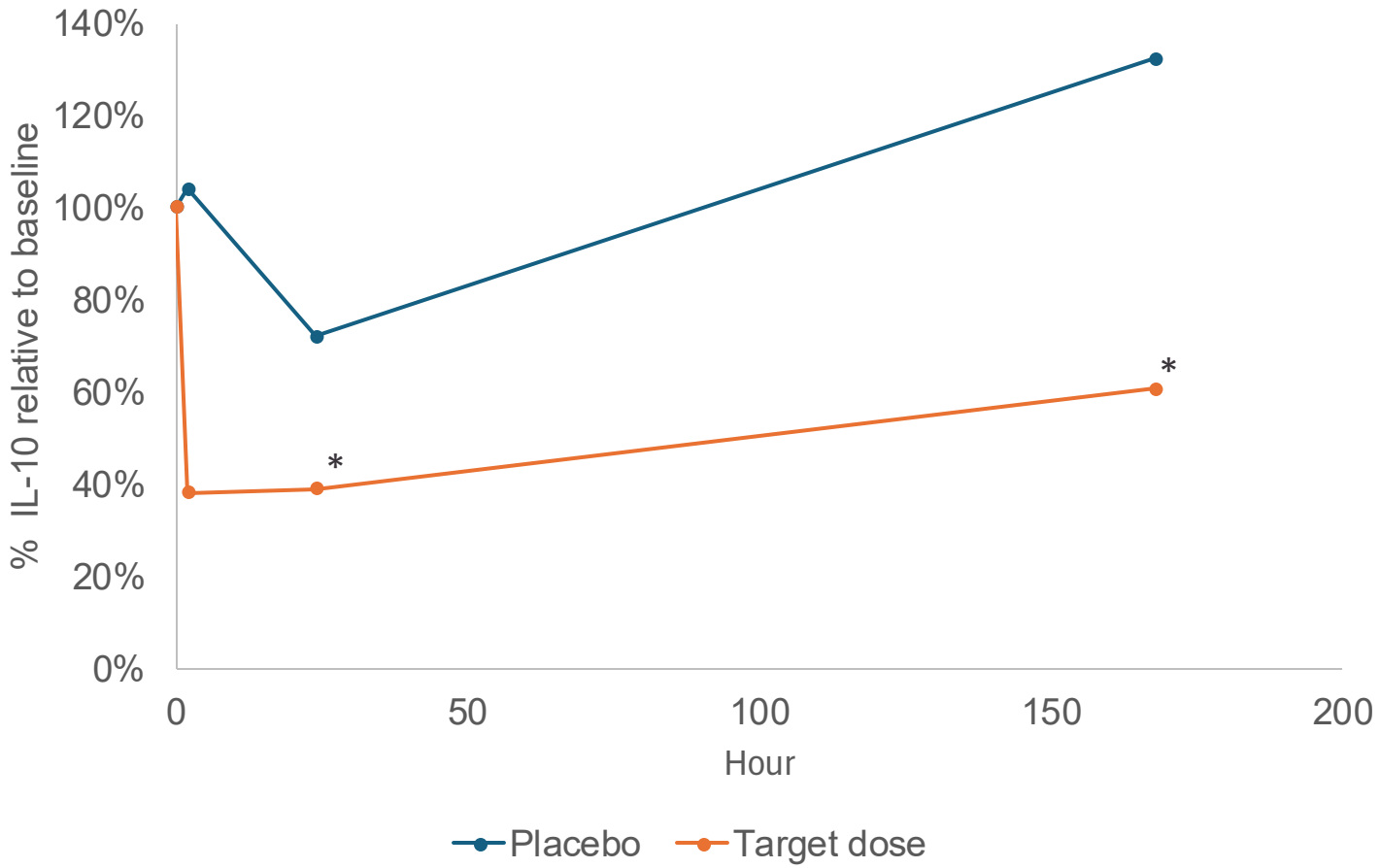
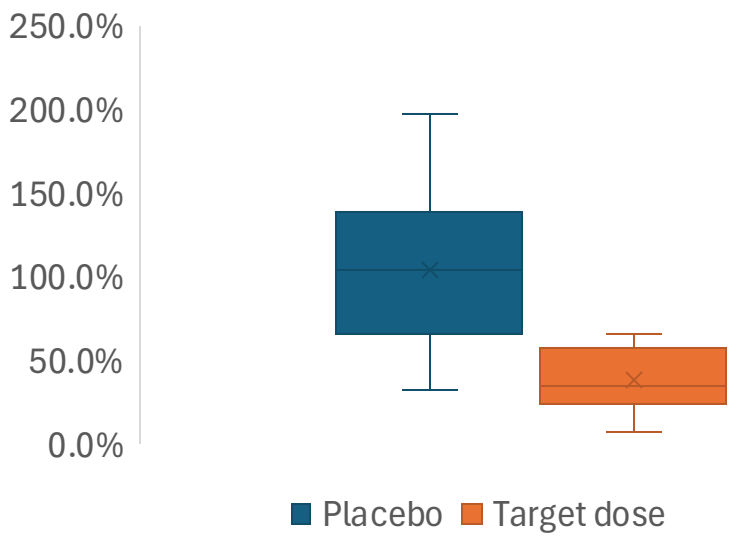
# Gemini significantly reduces IL-10 production compared to placebo

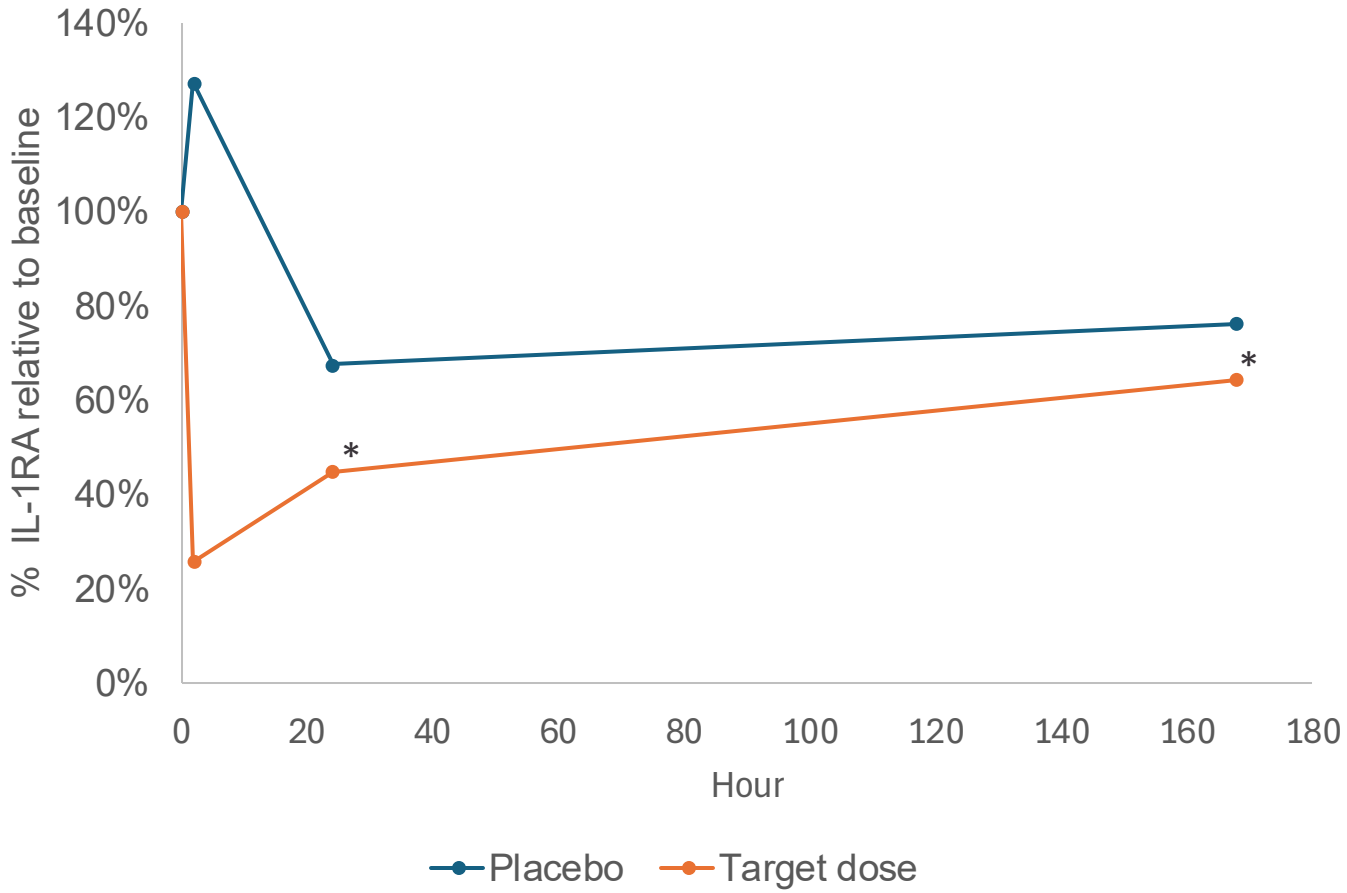


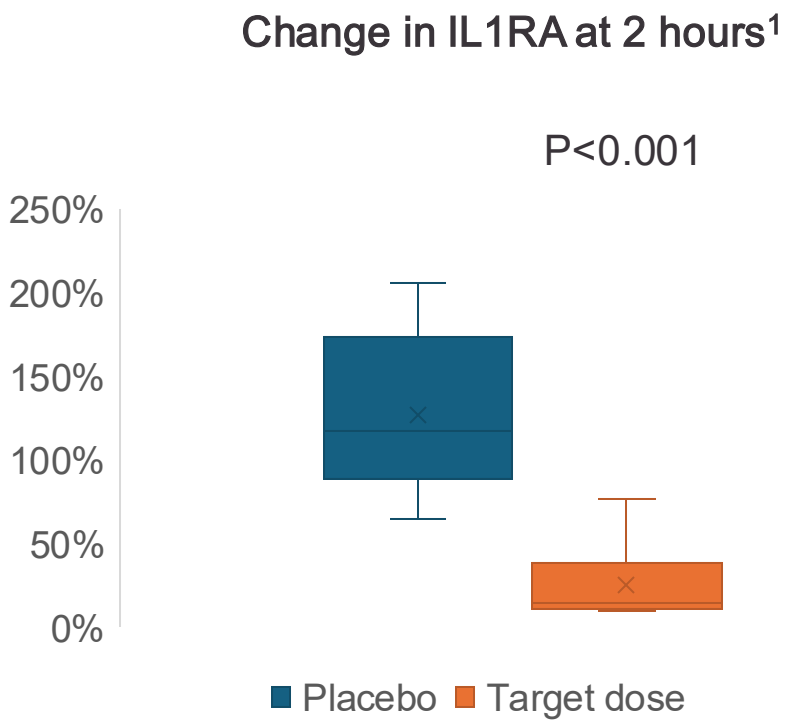

**Change in IL-10 at 2 hours[1]**




[1]p value based on 2-tailed t-test
*Reduction in IL-10 activity in treated group remains significantly below pre-dose baseline at 24 hours (p<0.0001) and 168 hours post dose (p <0.03), p values based on 1-tailed t-test

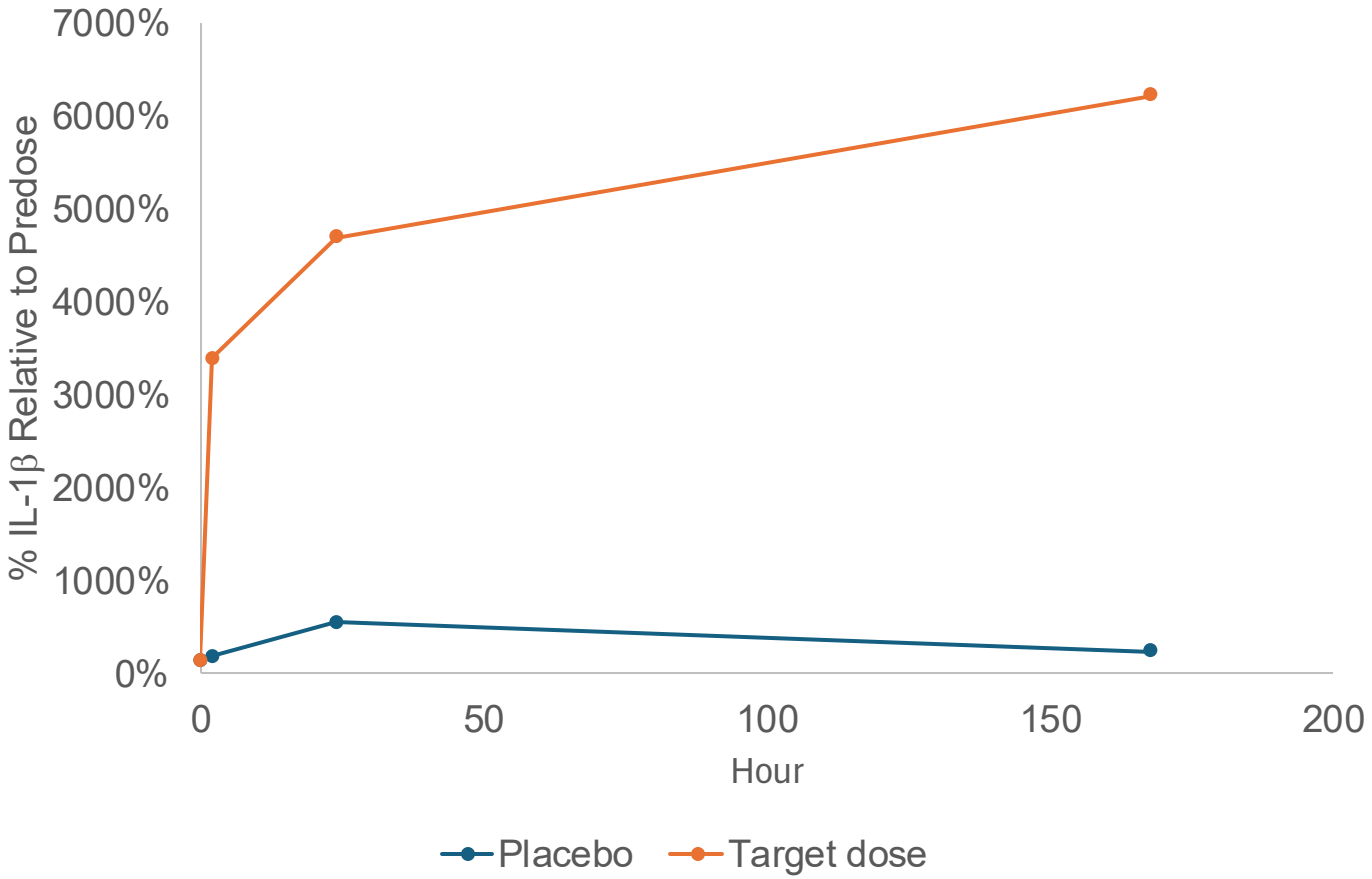
# Gemini significantly reduces IL-1RA production compared to placebo



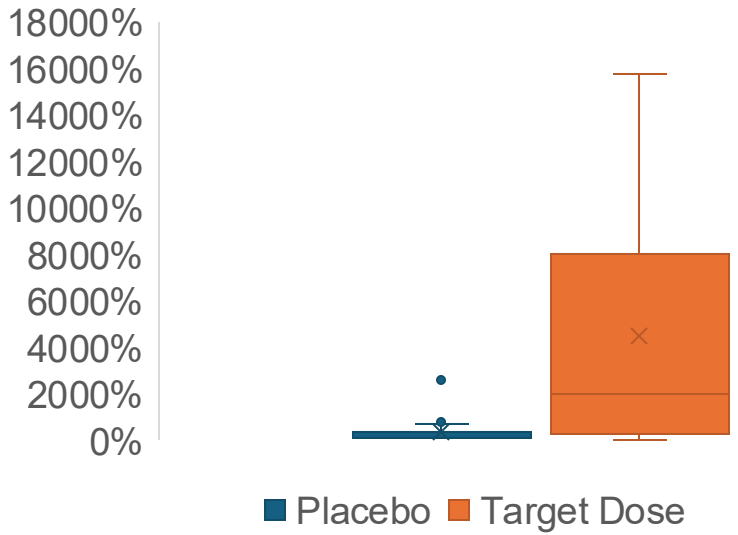

[1]p value based on 2-tailed t-test
*Reduction in IL-1RA activity in treated group remains significantly below pre-dose baseline at 24 hours (p<0.0001) and 168 hours post dose (p <0.02), p values based on 1-tailed t-test

# Gemini restored normal[1] PBMC IL-1β response to LPS stimulation



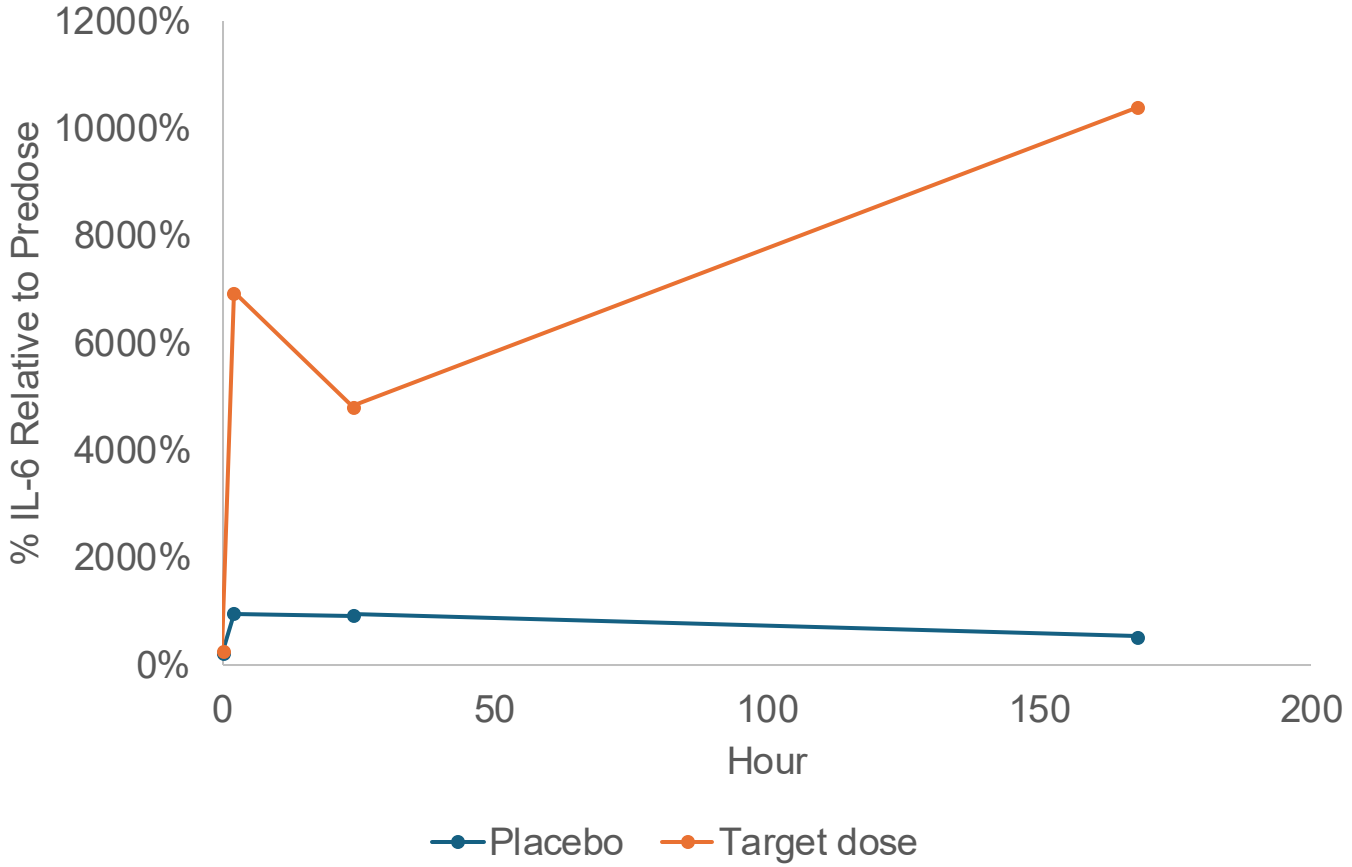

**Change in IL-1β response to LPS at all timepoints post dose**

P<0.0001[2]

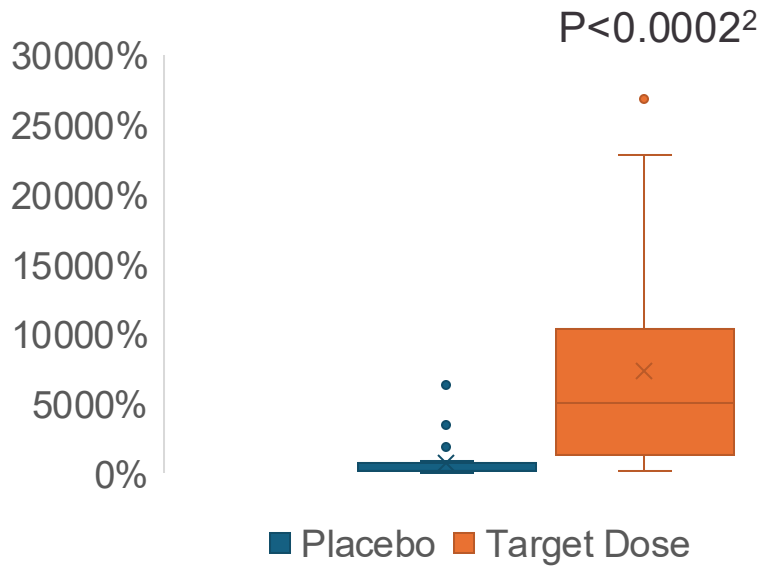



[1]Stimulation of PBMC from healthy individuals yields an approximate 8,000% increase in IL-1β
[2]p value based on 2-tailed t-test

# Gemini restored normal[1] PBMC IL-6 response to LPS stimulation

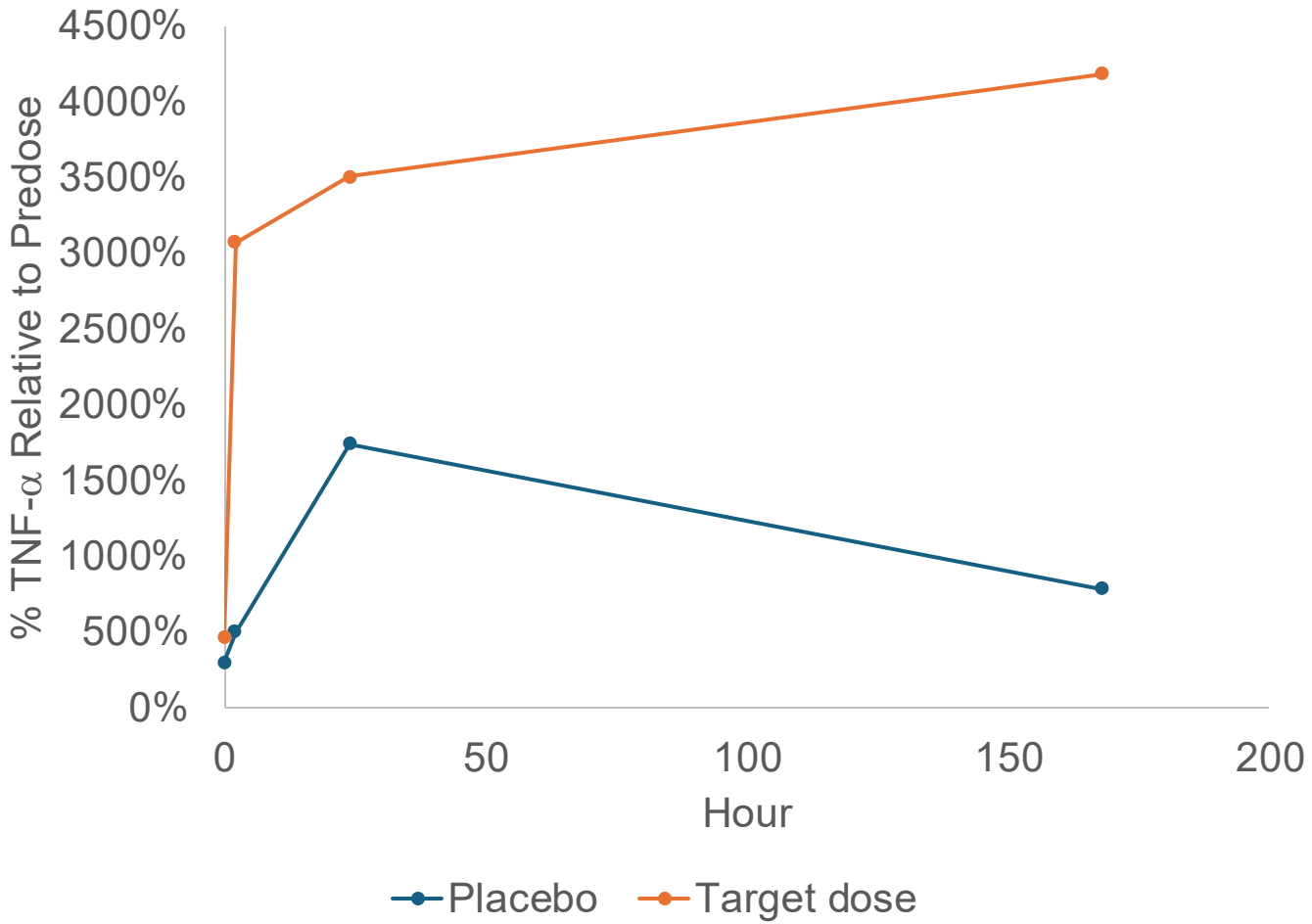



**Change in IL-6 response to LPS at all timepoints post dose**

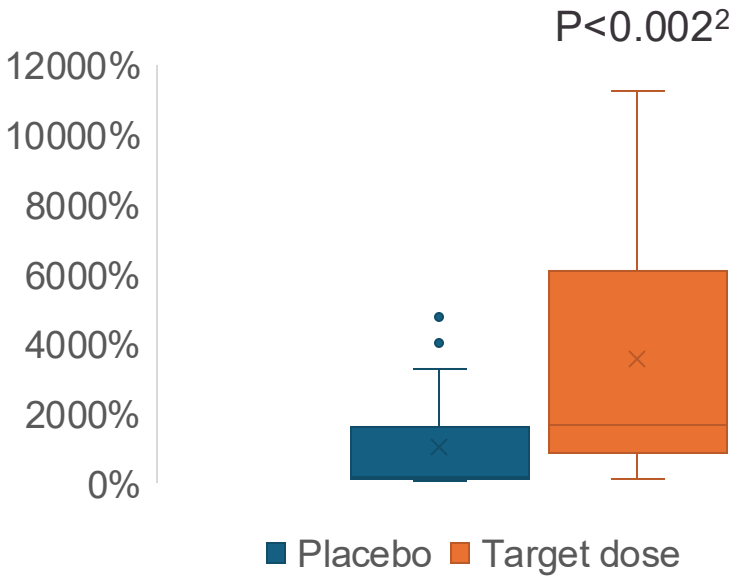



[1]Stimulation of PBMC from health individuals yields an approximate 14,000% increase in IL-6
[2]p value based on 2-tailed t-test

# Gemini restored normal[1] PBMC TNF-α response to LPS stimulation

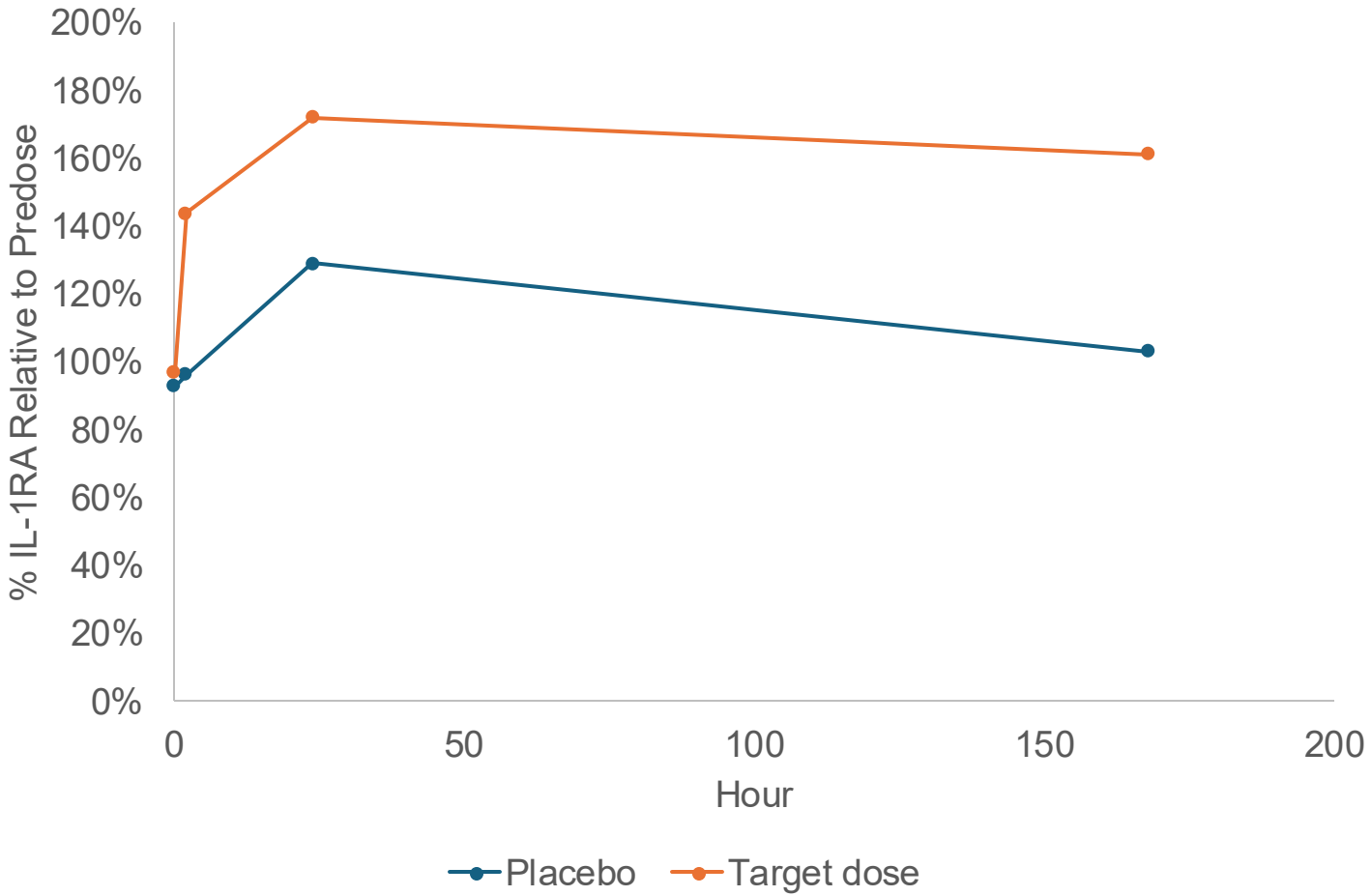



**Change in TNF-α response to LPS all time points post dose**



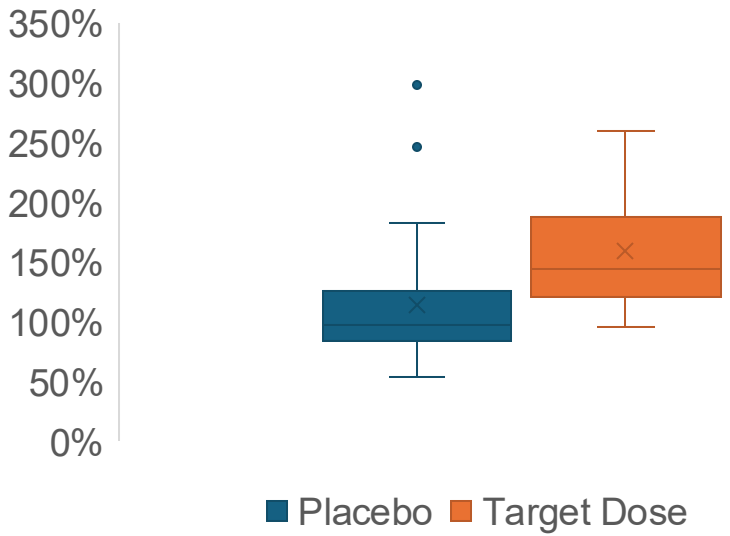

[1]Stimulation of PBMC from health individuals yields an approximate 9,750% increase in TNF-α
[2]p value based on 2-tailed t-test

# Gemini restored normal[1] PBMC IL-1RA response to LPS stimulation



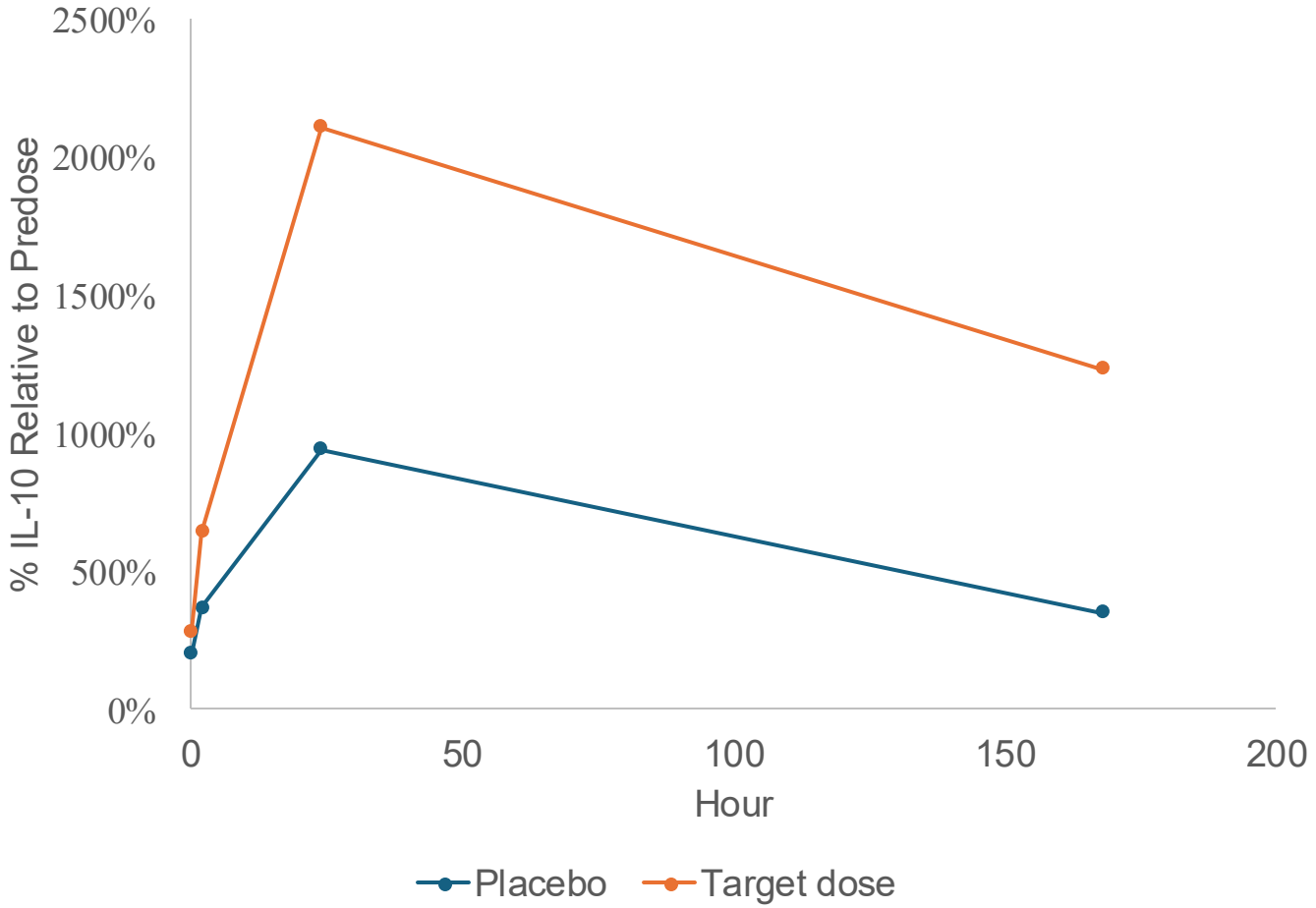

**Change in IL-1RA response to LPS at all timepoints post dose**

P<0.01[2]

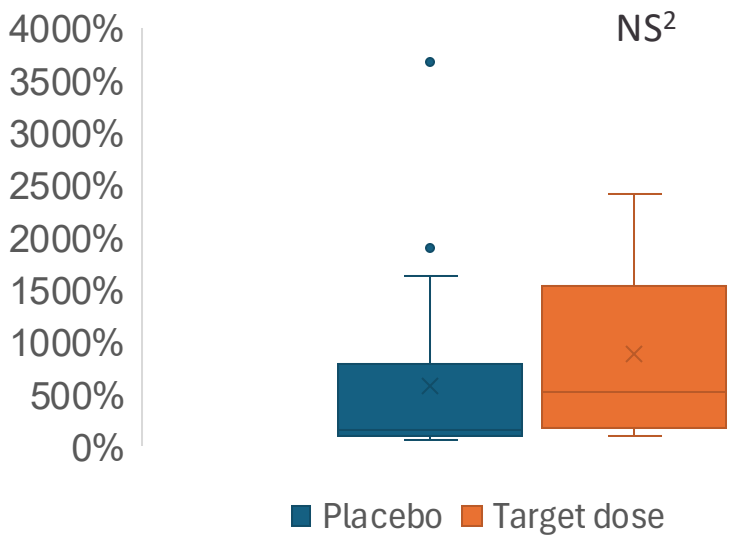



[1]Stimulation of PBMC from health individuals yields an approximate 430% increase in IL-1RA
[2]p value based on 2-tailed t-test

# Gemini restored normal[1] PBMC IL-10 response to LPS stimulation




**Change in IL-10 response to LPS at all time points post dose**

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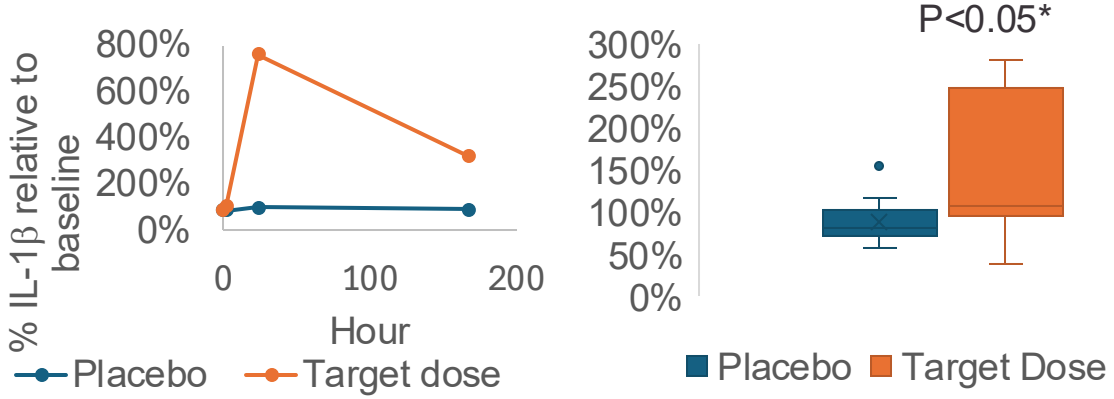
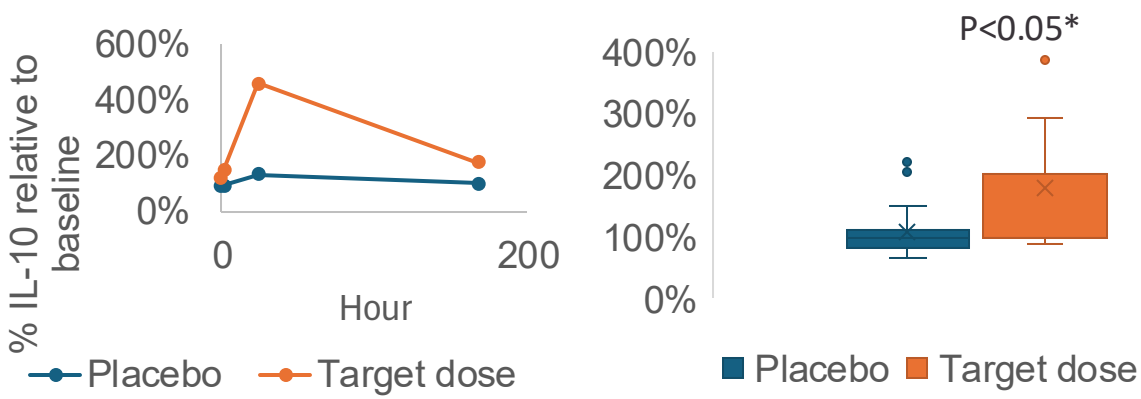
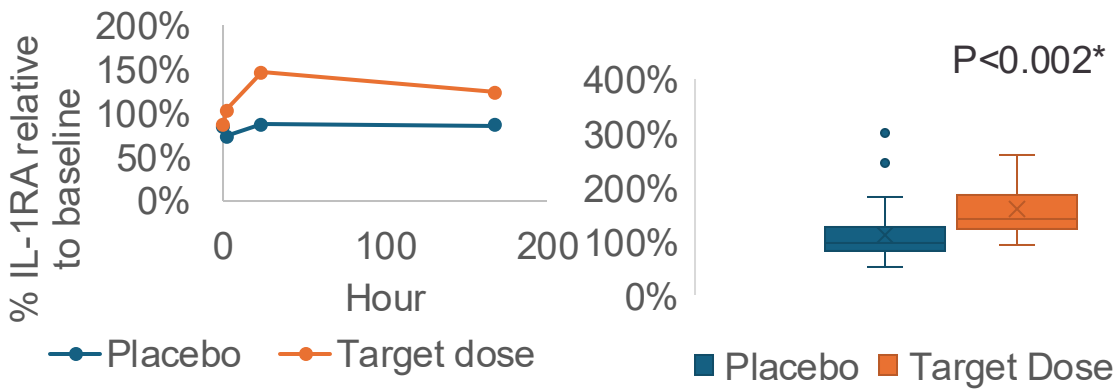
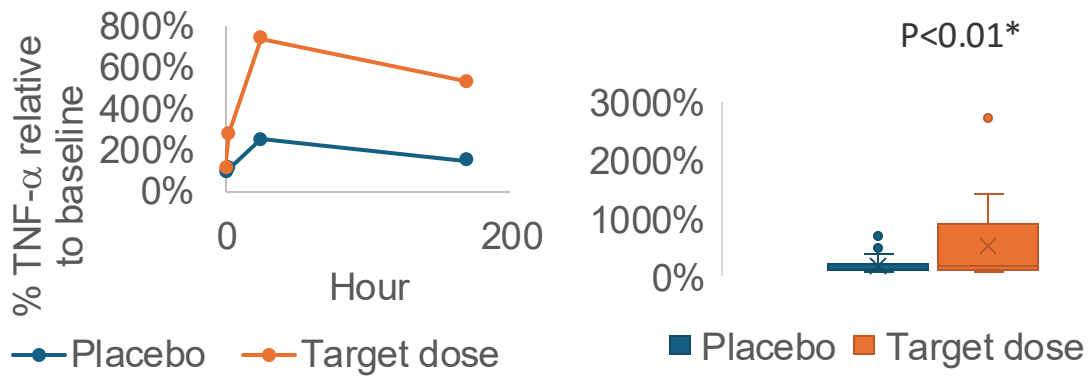
[1]Stimulation of PBMC from health individuals yields an approximate 1,400% increase in IL-10
[2]p value based on 2-tailed t-test

# Comparable results were observed for HMGB-1 stimulation



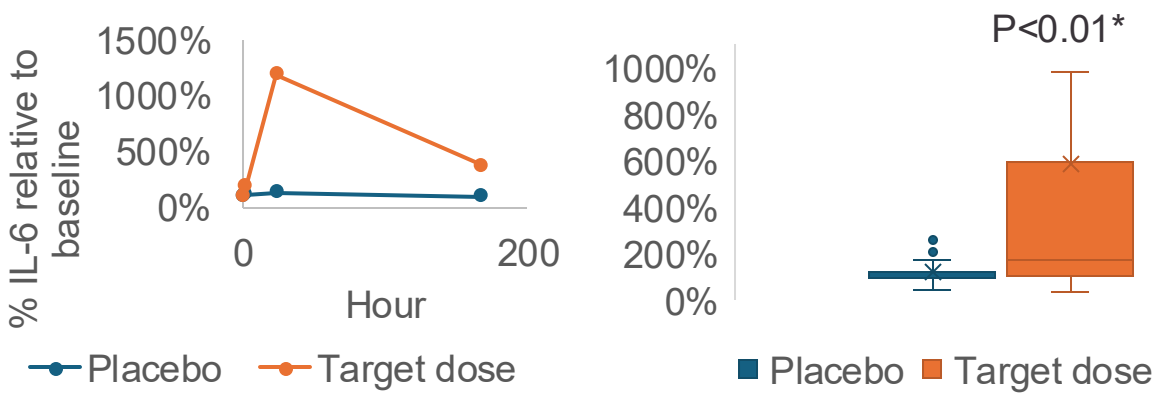




Normal response observed in healthy cells:

| | |
|---|---|
| IL-1β | 869% |
| IL-1RA | 371% |
| IL-10 | 178% |
| TNF-α | 3,546% |
| IL-6 | 3,989% |




*Change in response for all post dose time points vs placebo

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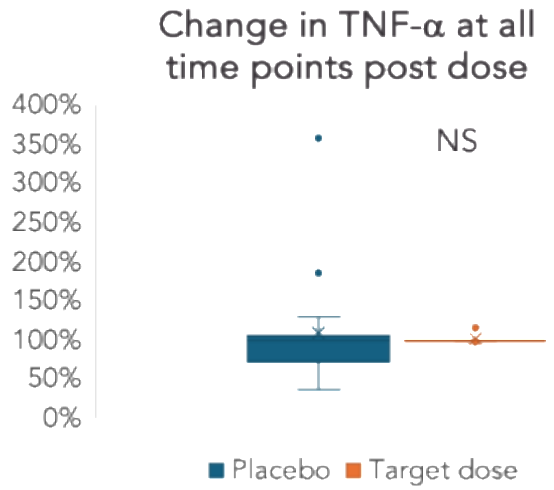
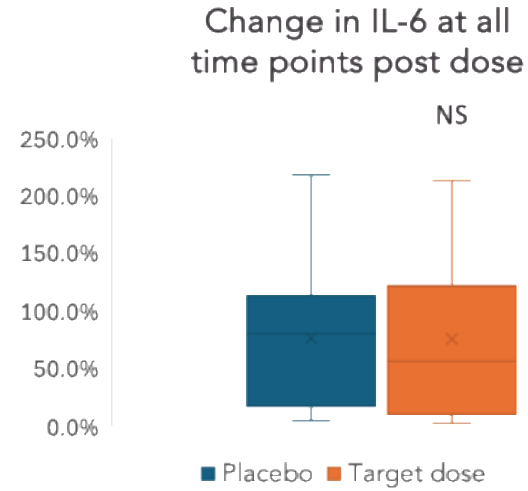
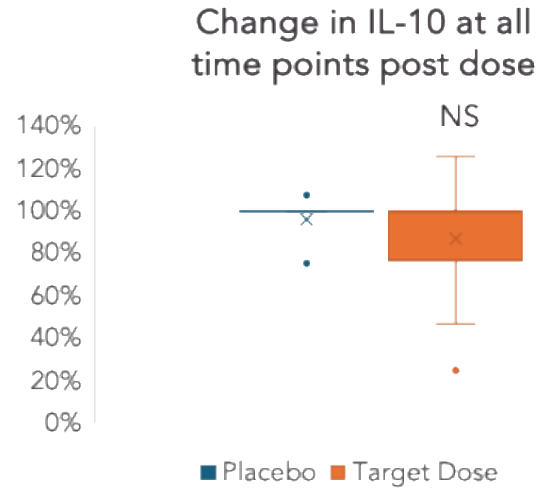
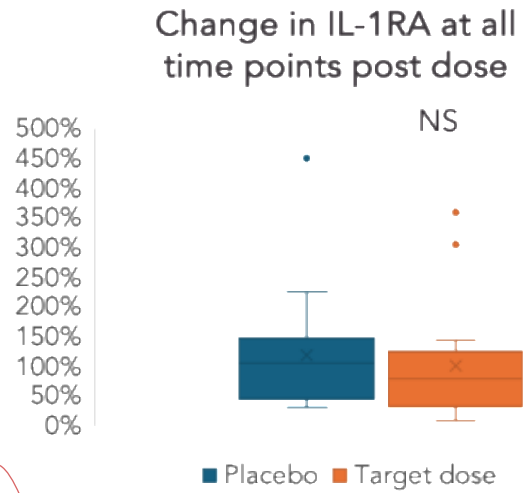
# Effect of Gemini on Patient PBMCs with Low Background Inflammation

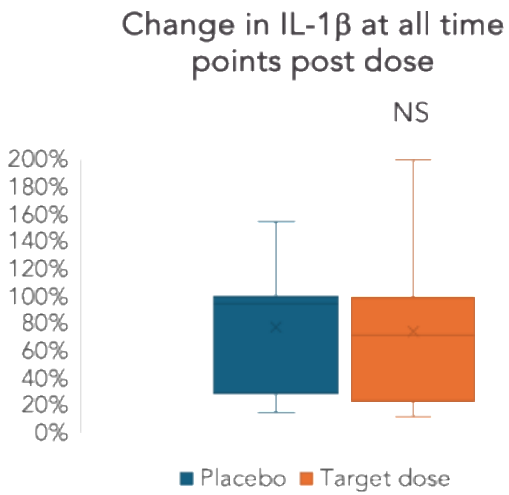
# As expected, Gemini does not increase inflammatory activity in low background patients[1]

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[1]p value based on 2-tailed t-test

# Safety Summary

# RVL-CKD01 Treatment Emergent Adverse Events

## Number of Total Events by Severity

| | Gemini Subtherapeutic dose N=6 | Gemini Low dose N=8 | Gemini Target dose N=12 | Gemini High dose N=6 | Placebo N=8 | Overall N = 40 |
|---|---|---|---|---|---|---|
| Mild (Grade I) | 3 | 2 | 8 | 2 | – | 15 |
| Moderate (Grade II) | – | 3 | 4 | 2 | 1 | 10 |
| Severe (Grade III) | – | – | – | 3 | – | 3 |
| Life-Threatening (Grade IV) | – | – | – | – | – | – |
| Death (Grade V) | – | – | – | – | – | – |
| **Total** | **3** | **5** | **12** | **7** | **1** | **28** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Related** | 1 | 3 | 6 | 7 | – | 17 |
| **Unrelated** | 2 | 2 | 6 | – | 1 | 11 |

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# RVL-CKD01 Treatment Emergent Adverse Events Related to Gemini

| | Adverse Event | Number of Events | Grade |
|---|---|---|---|
| **Subtherapeutic dose** | Headache/Head Pain | 1 | Mild (Grade I) |
| **Low dose** | Headache/Head Pain | 1 | (Moderate (Grade II) |
| | Dizziness | 1 | (Moderate (Grade II) |
| | Nausea | 1 | Mild (Grade I) |
| **Target dose** | Headache/Head Pain | 2 | Mild (Grade I) |
| | Chills | 2 | Mild (Grade I) |
| | Loose Stools | 1 | Mild (Grade I) |
| | Body Aches | 1 | Mild (Grade I) |
| **High dose** | Headache/Head Pain | 2 | 1 Mild (Grade I); 1 (Moderate (Grade II) |
| | Chills | 1 | Severe (Grade III) |
| | Fatigue | 1 | Mild (Grade I) |
| | Fever | 1 | (Moderate (Grade II) |
| | Nausea | 1 | Severe (Grade III) |
| | Vomiting | 1 | Severe (Grade III) |

# Key Takeaways

- Gemini corrects high background inflammation in patient PBMCs
  - High background PBMCs from untreated patients do not respond to stimulation (a form of immunoparalysis)
  - Gemini restores normal cell responsiveness to stimulation
  - The rebalancing effect is durable (out to one week post dose)
- Gemini has no significant effect on background inflammation when background is low (as expected)
- Gemini has an excellent safety profile to date
- **Gemini has the potential to TREAT patients with acute or chronic inflammatory conditions**

# Thank You!

For more information, please visit
www.revbiosciences.com