



Revolutionizing Data Exploration: An Interactive Journey through R Shiny

What's the secret formula for transforming dose
decision-making in the pharmaceutical industry?



Valentin Legras, Senior Data Scientist
F. Hoffmann-La Roche, Basel, Switzerland

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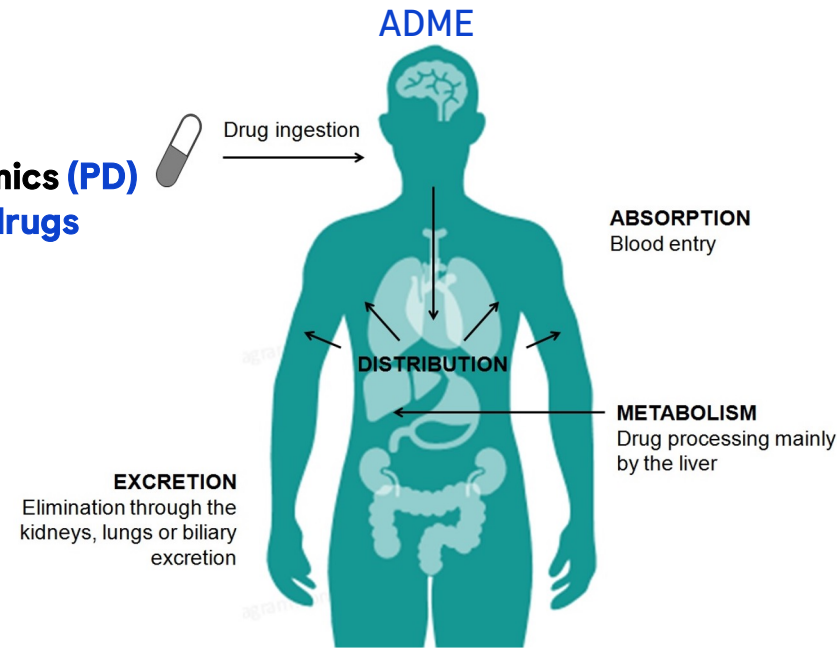
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- R Shiny application
- Safety use case
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Introduction

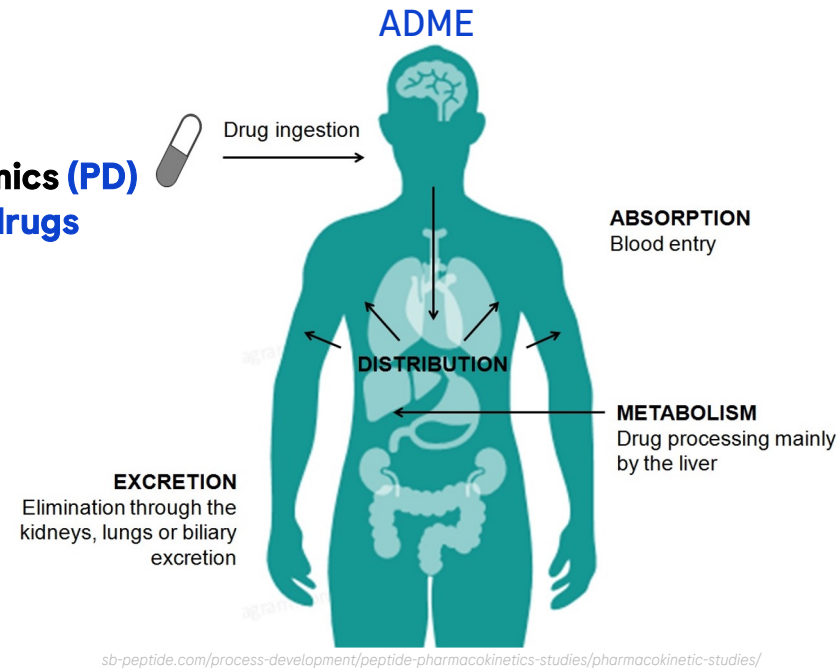
Introduction

- Focus on **pharmacokinetics (PK)** and **pharmacodynamics (PD)**
- two vital areas of study that provide insights into **how drugs interact with the human body**.



Introduction

- Focus on **pharmacokinetics (PK)** and **pharmacodynamics (PD)**
- two vital areas of study that provide insights into **how drugs interact with the human body**.



- Explore the key principles used in **PK/PD**, which are essential for the drug development to **better predict drug efficacy and safety**, and therefore improve patient outcomes.
- **R Shiny application** that simulate PK data and provide an interactive visualization. It allows clinicians and modelers to quickly **investigate multiple scenarios and get valuable insights** from clinical data.

Context

Data workflow



popPK dataset (Population Pharmacokinetic Analysis)

NONMEM: modelling software

CDISC = Clinical Data Interchange Standards Consortium

ADaM = Analysis Data Model

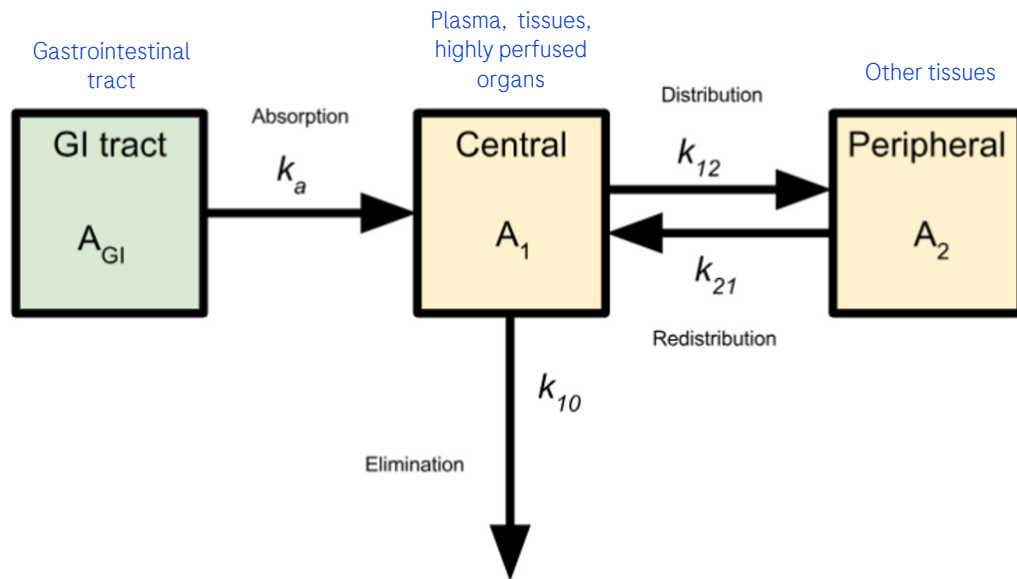
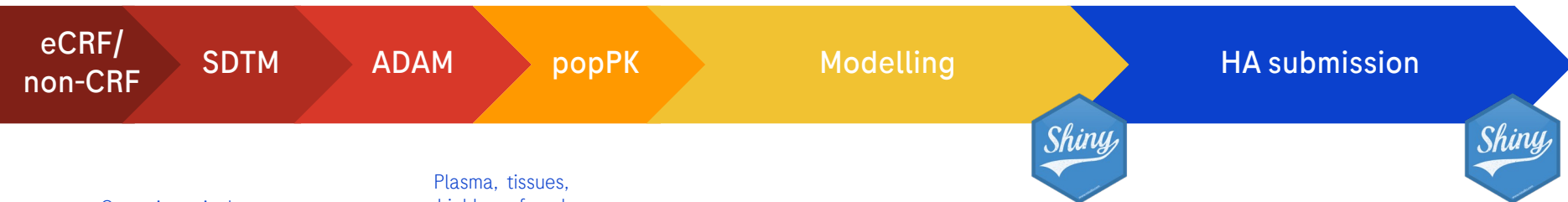
SDTM = Study Data Tabulation Model

eCRF = Electronic Case Report Form

Context

Modelling

Roche



Modelling

- Input: popPK dataset
- Translate ADME into a **mathematical model**
- **Fitting** of the data

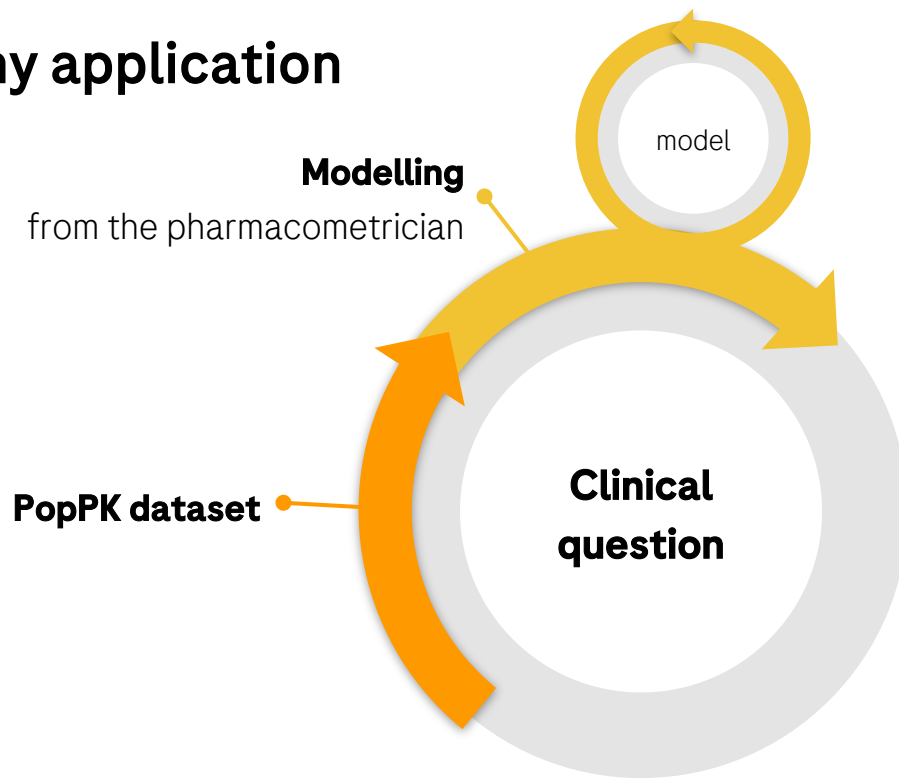
HA submission

- Datasets and specifications
- Modelling outputs
- TLGs

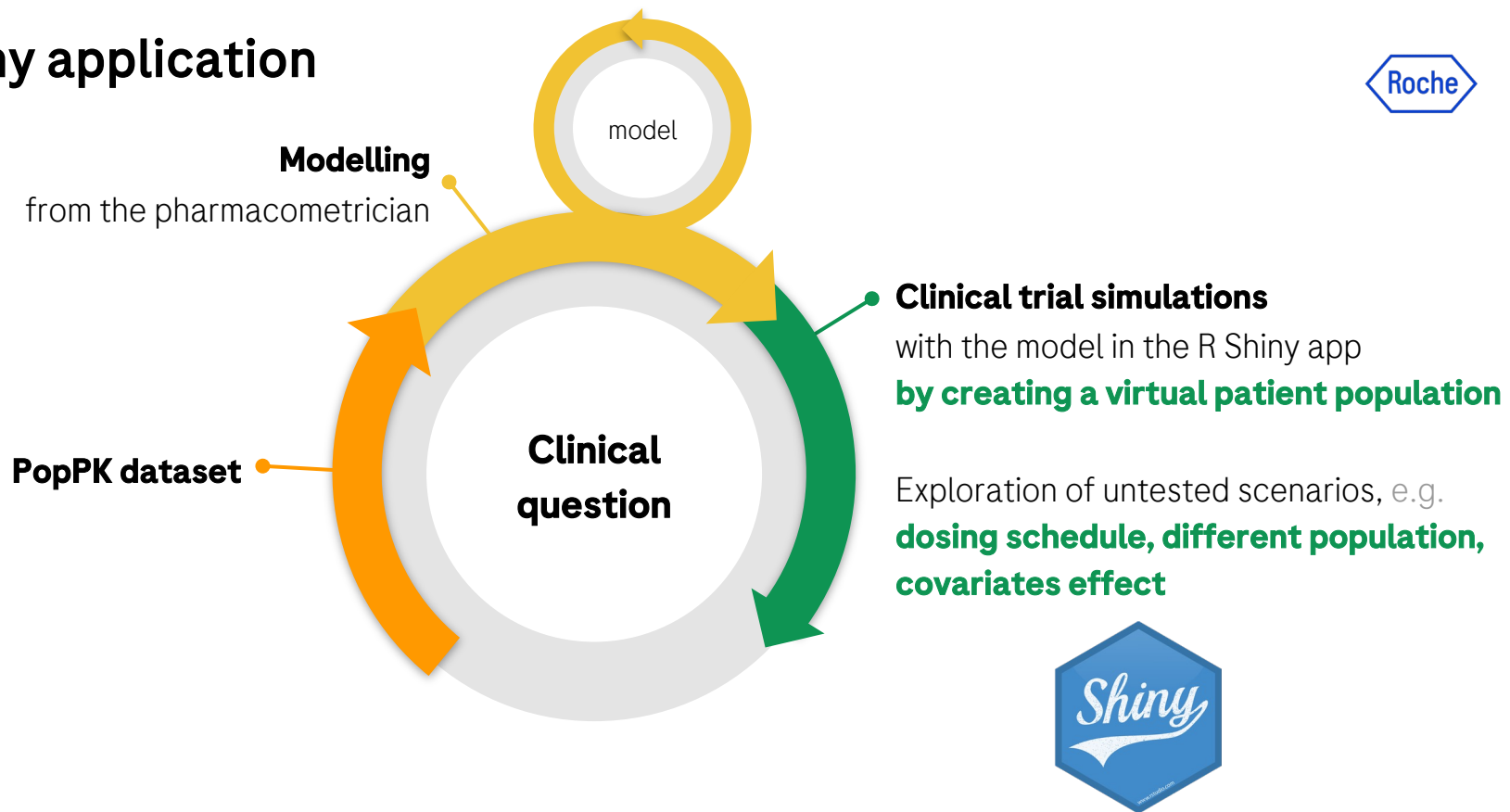
A_{GI} , A_1 and A_2 : amounts of drug
 k_a , k_{12} , k_{21} and k_{10} : rate constants

R Shiny application

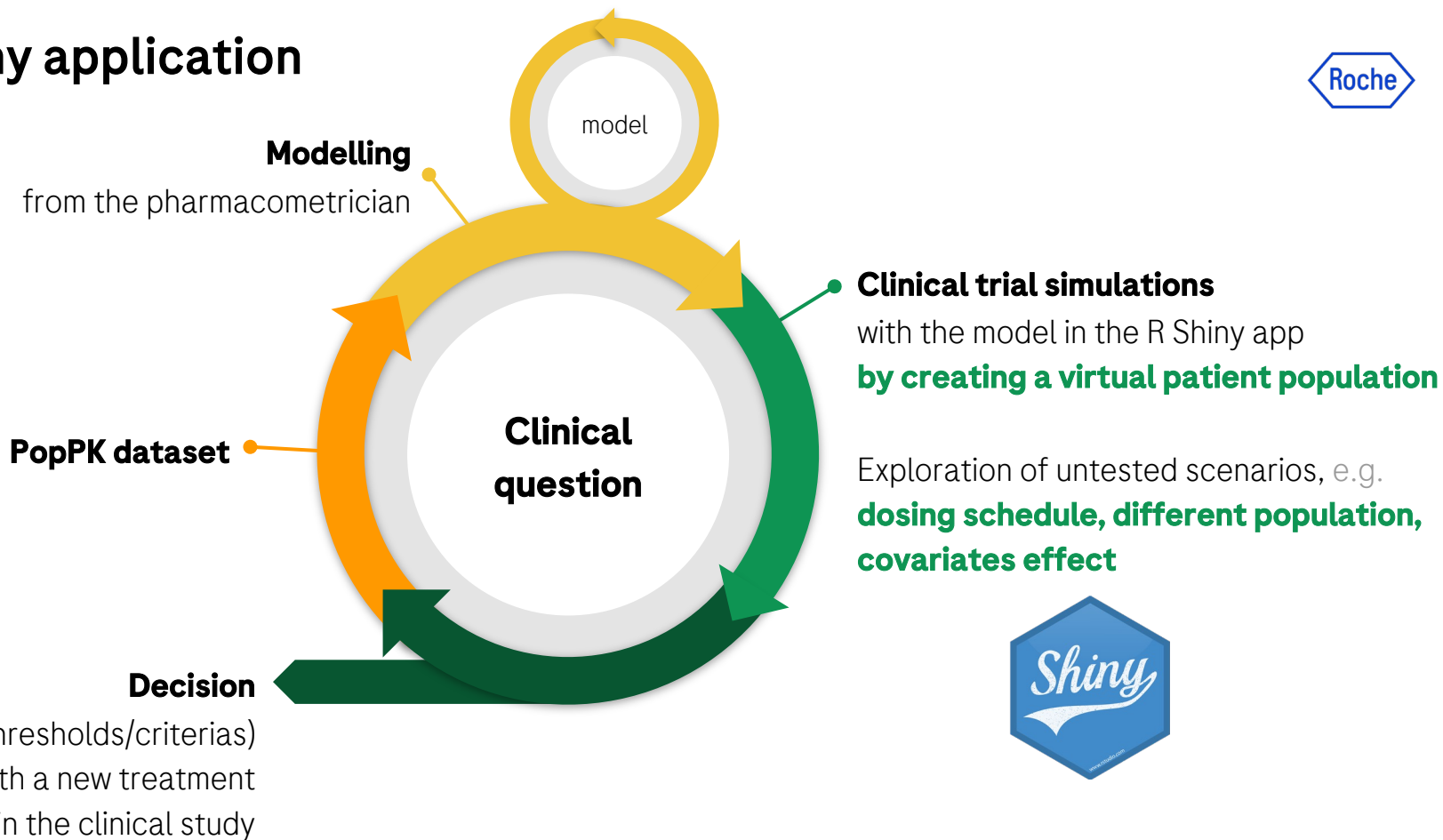
R Shiny application



R Shiny application



R Shiny application



Safety use case

Safety use case

Dose administration duration

FDA question: Demonstrate on the study population how much **infusion duration can be reduced (IV) without worsening the safety**, Infusion Related Reaction (IRR)

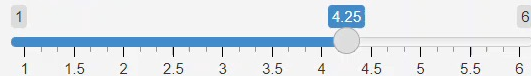
Seed Number

Number of simulated subjects:

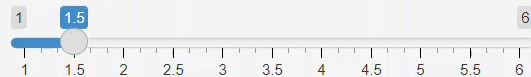
☒ Dose at Week 52 for Arm B & C☐ Dose at Week 50 for Arm A (and W50-80 of ARM C)

Duration of infusion (hour) for Arm B and C:

Week 0 Dose



Week 2 Dose



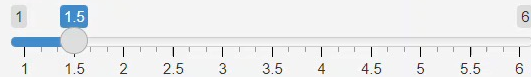
Week 24 Dose



Week 26 Dose



Week 52 Dose

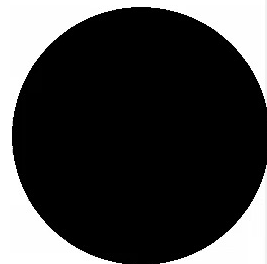


Covariate parameters:

Model Description

Model Scheme

Design



Safety use case

Dose administration duration

FDA question: Demonstrate on the study population how much **infusion duration can be reduced** (IV) **without worsening the safety**, Infusion Related Reaction (IRR)



Outcome: **FDA agreed** to continue in Phase 3 with this lower infusion duration
R Shiny app **contributed to not run a clinical study** to test these scenarios

Efficacy use case

Efficacy use case

Treating infection disease

Goal: Propose a **dosing schedule**, that ensures **90%** of patients to have a minimum concentration above the efficacy threshold ($C_{\min} \geq 150 \text{ ng/ml}$)

Insert Observed Data (xlsx file)

Browse...

No file selected

Simulation settings

Treatment duration (days)

5

Day 1 first dose (mg)

0

550

2,200

Day 1 second dose (mg)

0

550

2,200

Maintenance doses (mg)

0

550

2,200

Dosing Regimen

☐ QD ☒ BID

Prediction interval

☒ 80% ☐ 90% ☐ 95%

Plots

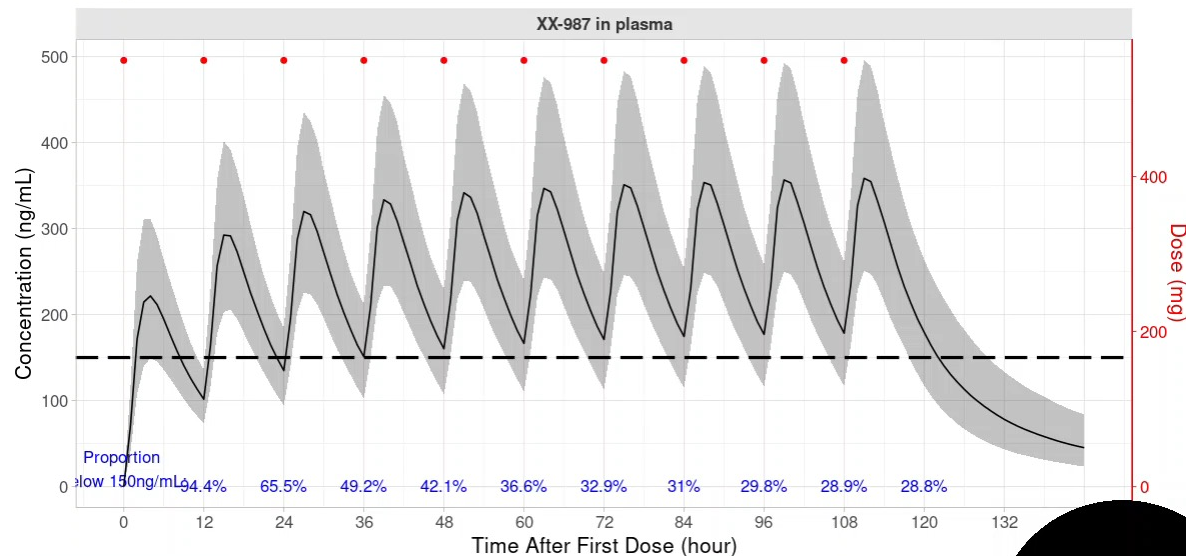
Tables

Model

Summary

Cmin

Simulated Median with 80% Prediction Interval



Download Plot

Efficacy use case

Treating infection disease

Goal: Propose a **dosing schedule**, that ensures **90%** of patients to have a minimum concentration above the efficacy threshold ($C_{\min} \geq 150$ ng/ml)



Outcome: Impact on the dose decision-making:

Selection of a Phase 3 study with a dosing schedule of **825 mg, twice a day**

Conclusion

Conclusion

- As Data Scientist, we develop R Shiny apps for **clinical trial simulation** to **support dose decision-making** in clinical studies
- Powerful tool to **enhance communication** with Clinical teams of our modelling results, **interface** between clinical team and data scientist/modeler
- Very helpful for **flexible** and **real time clinical data simulation** that guides **dose decision-making**
- Illustrate **drug efficacy** and **safety** in clinical studies, gives us clear idea on how to **plan/extend clinical studies**
- **Shiny apps** and **its interactive visualization** are more and more used across the Pharmaceutical industries



Doing now what patients need next

Insert Observed Data (xlsx file)

Browse...

No file selected

Simulation settings

Treatment duration (days)

5

Day 1 first dose (mg)



Day 1 second dose (mg)



Maintenance doses (mg)



Dosing Regimen

☐ QD ☒ BID

Prediction interval

☒ 80 % ☐ 90 % ☐ 95 %

rBA Factor

1

Percentage of fed patients

100

Lung to plasma ratio

1,05

Additional Analyte

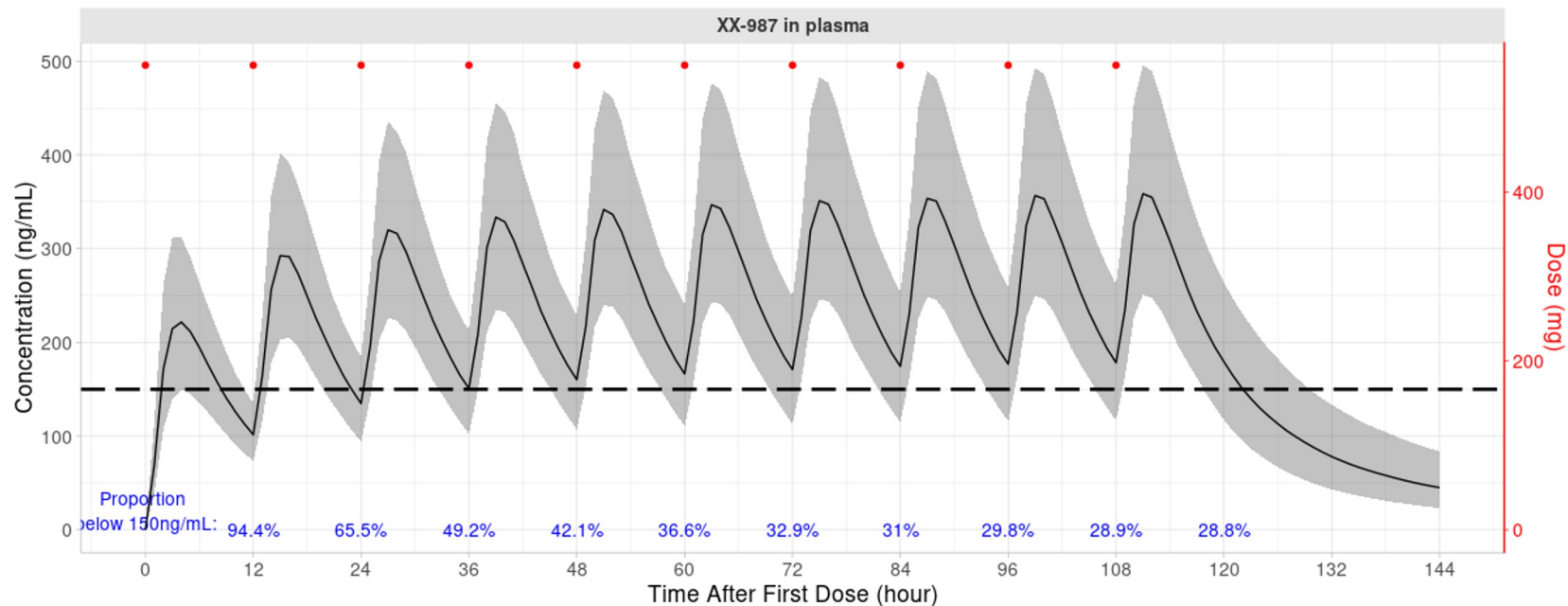
None

☒ Show Y-axis doses

Run Simulation

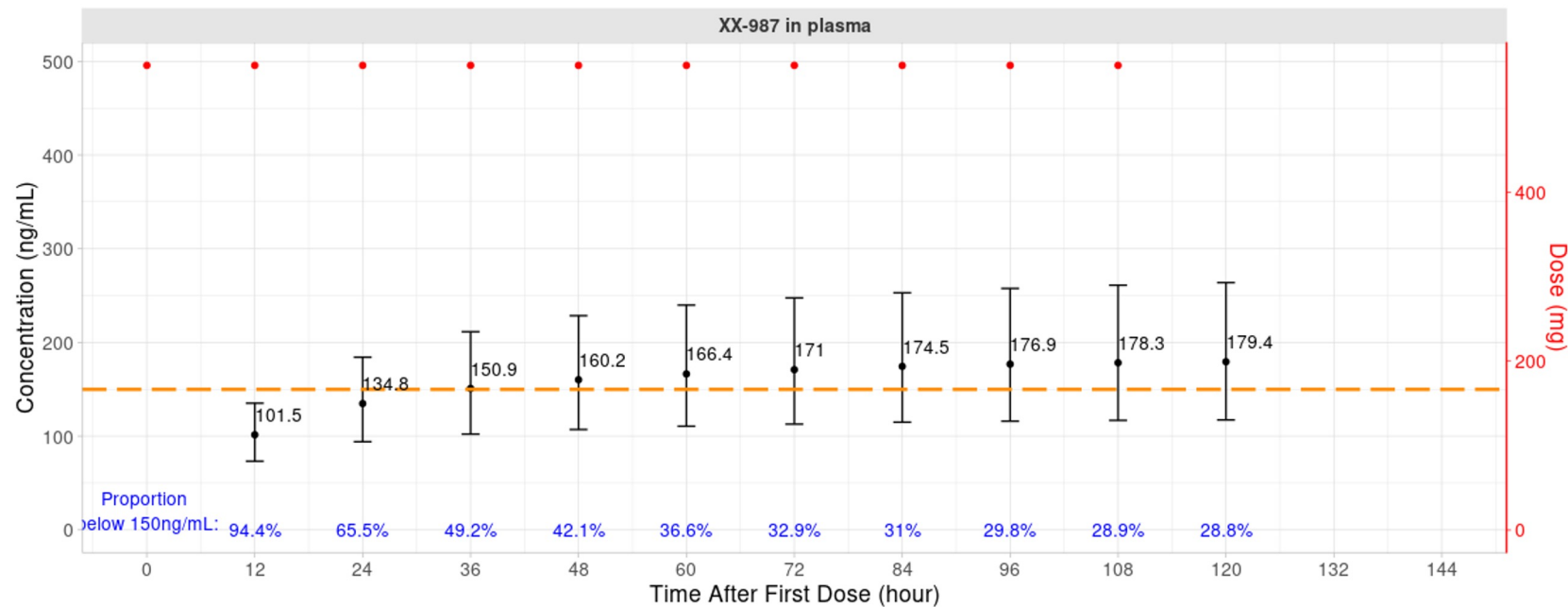
[Plots](#)[Tables](#)[Model](#)[Summary](#)[Cmin](#)

Simulated Median with 80% Prediction Interval

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Simulated Median with 80% Prediction Interval

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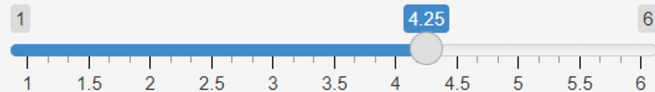
[Plots](#)[Tables](#)[Model](#)[Dosing History](#)[Ctrough Statistics](#)[Observed VS Simulated Data](#)Show entries

Search:

	Time since first dose (h) ⬆️	Analyte ⬆️	P10 ⬆️	P50 ⬆️	P90 ⬆️
1	12	XX-987 in plasma	73.2697727392479	101.48880489644	135.153443814284
2	24	XX-987 in plasma	94.1009496734054	134.797649474349	184.269810337842
3	36	XX-987 in plasma	102.20874959413	150.901617170966	211.477542830661
4	48	XX-987 in plasma	107.127968177587	160.208232016913	228.538973191176
5	60	XX-987 in plasma	110.598805087666	166.411576002036	239.8722239891
6	72	XX-987 in plasma	112.844457688471	170.981344168375	247.547171453719
7	84	XX-987 in plasma	114.934915937641	174.477525640084	253.039457685777
8	96	XX-987 in plasma	116.066981541952	176.870737786208	257.694801120979
9	108	XX-987 in plasma	116.855506459463	178.322989660456	261.055018665819
10	120	XX-987 in plasma	117.323740515619	179.42892191763	263.904180781944

Showing 1 to 10 of 10 entries

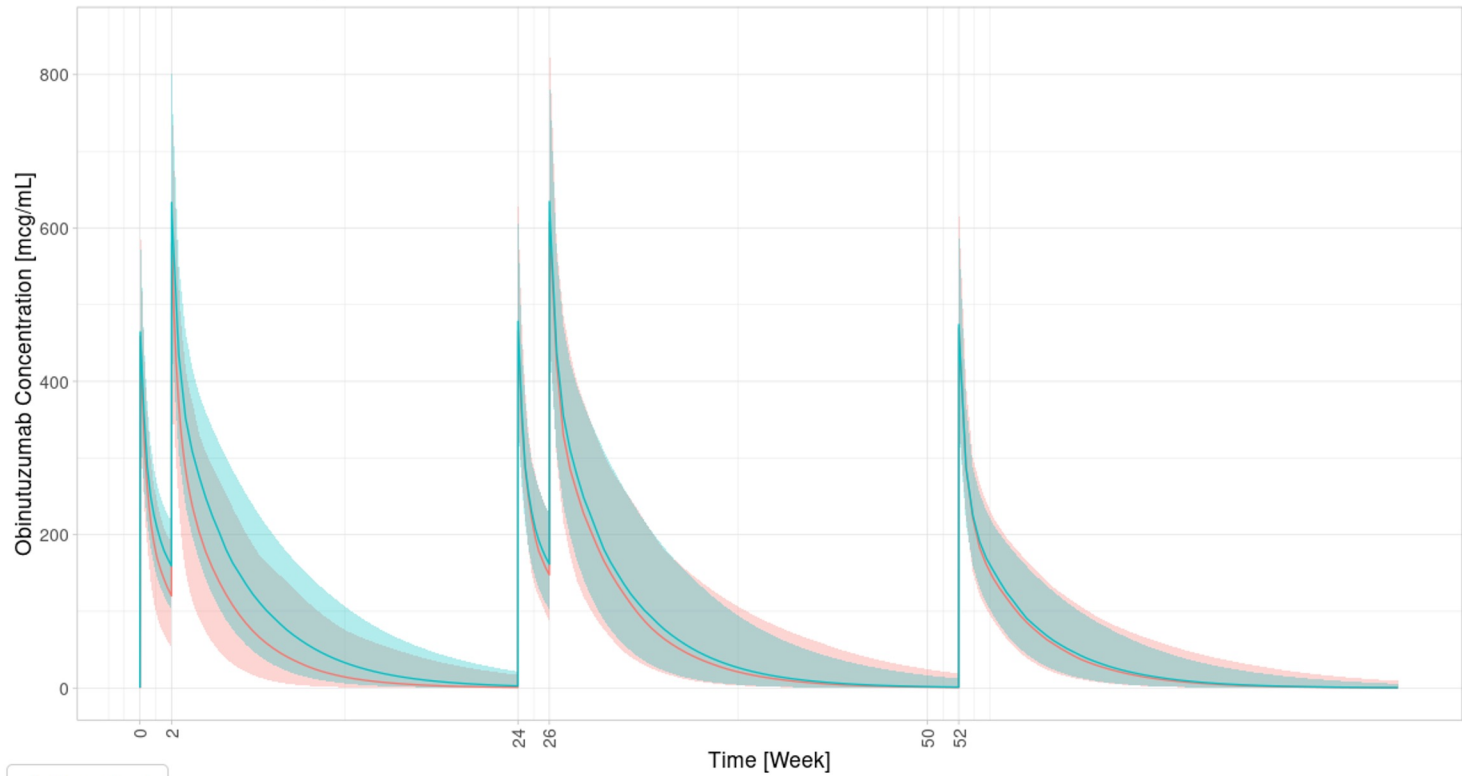
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Seed Number**Number of simulated subjects:**☒ Dose at Week 52 for Arm B & C☐ Dose at Week 50 for Arm A (and W50-80 of ARM C)**Duration of infusion (hour) for Arm B and C:****Week 0 Dose****Week 2 Dose****Week 24 Dose****Week 26 Dose****Week 52 Dose****Covariate parameters:****Mean of Weight (kg)****SD of Weight****Mean of Albumin (g/L)****SD of Albumin****Mean of IgG (g/L)****SD of IgG**

PK Profile

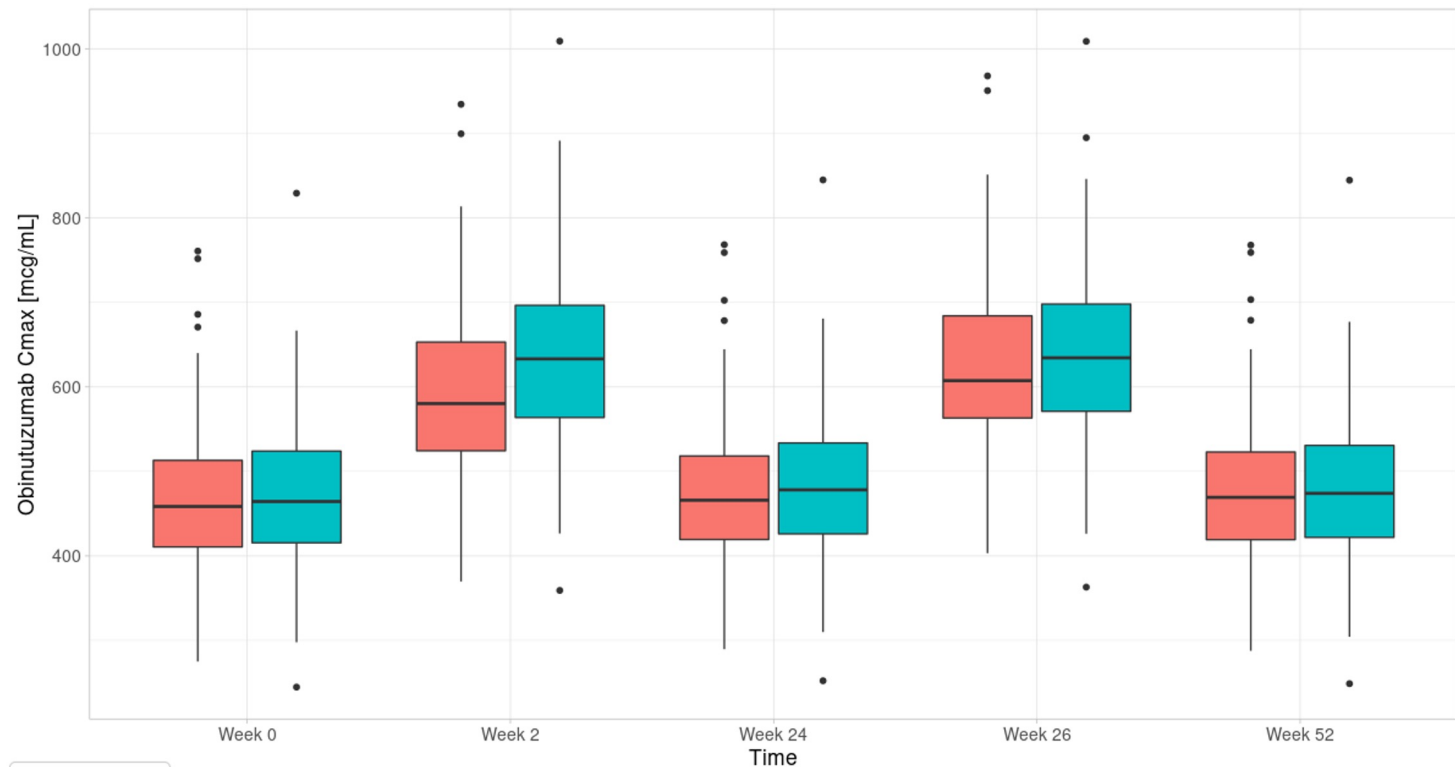
C_{max}C_{min}

Simulated PK Profile, Median with 90% Prediction Interval

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Duration of infusion [h] (Arm A) = 4.25 [Week 0], 3.25 [Week 2], 3.25 [Week 24], 3.25 [Week 26], 3.25 [Week 52]
Duration of infusion [h] (Arm B & C) = 4.25 [Week 0], 1.5 [Week 2], 1.5 [Week 24], 1.5 [Week 26], 1.5 [Week 52],

Simulated Cmax

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Scenario Arm A Arm B

Duration of infusion [h] (Arm A) = 4.25 [Week 0], 3.25 [Week 2], 3.25 [Week 24], 3.25 [Week 26], 3.25 [Week 52]
Duration of infusion [h] (Arm B & C) = 4.25 [Week 0], 1.5 [Week 2], 1.5 [Week 24], 1.5 [Week 26], 1.5 [Week 52],

Show entries

Search:

	Dose Week	Tmax (day)	Scenario	N	Arithmetic Mean (SD)	Median (P5 - P95)	Geometric Mean (Geometric CV%)
1	Week 0	0.177	Arm A	100	473.56 (91.34)	458.52 (340.6 - 618.44)	465.21 (19.06 %)
2	Week 0	0.177	Arm B	100	469.56 (85.86)	464.34 (342.77 - 598.52)	461.85 (18.58 %)
3	Week 0	0.177	Arm C	100	465.61 (106.43)	448.92 (321.63 - 702.05)	454.33 (22.37 %)
4	Week 2	14.062	Arm B	100	630.41 (107.45)	633.24 (452.99 - 806.42)	621.24 (17.5 %)
5	Week 2	14.062	Arm C	100	593.63 (121.58)	576.12 (415.82 - 837.94)	581.93 (20.15 %)
6	Week 2	14.135	Arm A	100	593.49 (108.77)	580.34 (434.16 - 797.27)	583.94 (18.21 %)
7	Week 24	168.062	Arm B	100	480.12 (87.89)	478.22 (347.16 - 610.67)	472.21 (18.62 %)
8	Week 24	168.062	Arm C	100	477.02 (107.16)	461.4 (328 - 713.08)	465.88 (21.94 %)
9	Week 24	168.135	Arm A	100	480.84 (91.74)	465.92 (348.08 - 627.52)	472.57 (18.8 %)
10	Week 26	182.062	Arm B	100	634.01 (109.11)	634.47 (453.08 - 810.64)	624.61 (17.67 %)
11	Week 26	182.062	Arm C	100	630.75 (124.16)	611.01 (459.07 - 878.47)	619.21 (19.4 %)
12	Week 26	182.135	Arm A	100	630.97 (113.62)	607.49 (466.48 - 846.18)	621.21 (17.83 %)
13	Week 52	364.062	Arm B	100	477.35 (87.76)	474.01 (346.69 - 607.04)	469.43 (18.69 %)
14	Week 52	364.062	Arm C	100	477.75 (106.7)	464.84 (327.78 - 713.07)	466.71 (21.82 %)
15	Week 52	364.135	Arm A	100	481.82 (91.96)	469.26 (348.07 - 629.3)	473.49 (18.86 %)

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