Statistical Analysis Plan

Sponsor:	Global Blood Therapeutics Inc., a wholly owned subsidiary of Pfizer
Protocol No:	GBT021601-013
Protocol Title:	A PHASE 1 STUDY TO ASSESS THE MASS BALANCE, EXCRETION, AND PHARMACOKINETICS OF [^{14}C]-GBT021601, AN ORAL HEMOGLOBIN S POLYMERIZATION INHIBITOR, IN HEALTHY PARTICIPANTS
PRA Project ID:	GBT2180A-2180AX
Version Date:	01-May-2023

1.0 Approvals

The Statistical Analysis Plan has been approved for use in this study.

Approver names have been redacted so as not to disclose personal information.

2.0 Table of Contents

3.0 Introduction

This Statistical Analysis Plan (SAP) describes the statistical methods that will be used during the analysis and reporting of data collected under Global Blood Therapeutics (GBT), Inc., Protocol GBT021601-013.

This SAP should be read in conjunction with the clinical study protocol and electronic case report form (eCRF). This version of the plan has been developed using the protocol Version 3.0, dated 13-Mar-2023 (including all amendments up to this protocol date) and the final eCRF(s) dated 31-Oct-2022.

An approved and signed SAP is a requirement for database lock.

This SAP only covers the results that will be processed by the ICON Early Development Services (EDS) Biostatistics Department, Statistical Programming Department and Pharmacokinetic Department.

ICON EDS will perform the pharmacokinetic (PK), and safety and tolerability evaluation.

Metabolic profiling is not described in this SAP and will not be included in the corresponding TFLs.
This SAP supersedes the statistical considerations identified in the protocol; where considerations are substantially different, they will be so identified. Any post-hoc or unplanned analyses, or significant changes from the planned analysis in this SAP performed to provide results for inclusion in the clinical study report (CSR) but not included in this SAP, will be clearly identified in Section 9.8.2 of the CSR. Changes to planned analyses do not require an updated SAP but should be included in the CSR if significant.

4.0 Changes from Previous Version of Approved SAP

This is the first version of the SAP.

5.0 Study Objectives

5.1 Primary

- To determine the whole blood and plasma concentrations of ^{14}C-GBT021601 total radioactivity.
- To assess the mass balance by determining ^{14}C-GBT021601 total radioactivity excreted in urine and feces.
- To determine the PK of GBT021601 in whole blood, plasma, and urine.

5.1.1 Primary Endpoint

- Concentrations of GBT021601 and of ^{14}C-GBT021601 total radioactivity in whole blood and plasma
- Amount and fraction of ^{14}C-GBT021601 total radioactivity dose excreted in urine, feces, emesis (if produced).
- PK parameters of GBT021601 and ^{14}C-GBT021601 total radioactivity, as feasible, in whole blood and plasma ($AUC_{0\text{-}24}$, $AUC_{0\text{-}last}$, $AUC_{0\text{-}inf}$, C_{max}, T_{max}, $T_{1/2}$, CL_R, CL/F, and V_z/F, if possible, and any other PK parameters as appropriate).
- Distribution of ^{14}C- GBT021601 total radioactivity in urine and feces.

5.2 Secondary

- To assess the safety and tolerability of GBT021601 administration in healthy participants.
- To characterize and identify metabolites of ^{14}C-GBT021601 in whole blood, plasma, urine, and feces.

5.2.1 Secondary Endpoint

- Incidence and severity of adverse events (AEs).
- Other safety results: clinical laboratory results, vital signs, 12-lead electrocardiogram (ECG) and physical examinations.

- Metabolite profiling is not covered in this SAP.

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6.0 Study Design

This Phase 1, single-center, open-label study will be conducted to evaluate the absorption, distribution, metabolism, and excretion (ADME) of GBT021601 in 8 to 10 healthy male or female participants. GBT021601 will be administered as a single oral dose of 200 mg GBT021601, containing ~74 kBq (~2 µCi) of ^{14}C-GBT021601, under fasted conditions.

After dosing on Day 1, blood (whole blood and plasma) and excreta (urine and feces) will be collected for up to 7 months due to the long elimination half-life from blood and plasma (approximately 28 to 30 days) of GBT021601, depending on how much radioactivity is recovered in excreta and the rate of elimination of radioactivity. Vomitus will be collected, if possible, if a participant vomits within 24 hours after study drug administration. Participants will remain confined in the clinical research unit (CRU) until discharge on Day 29. After discharge from the CRU, participants will return to the CRU for up to 11 visits. Each follow-up visit to collect blood and excreta will be a 24-hour stay in the CRU.

Concentrations of total radioactivity excreta will be assayed on a periodic basis to enable the Sponsor/Investigator to determine how long samples should be collected. Criteria for ending the collection of blood and excreta in a participant after Day 29 are: 1) ≥90% of the administered radioactive dose is recovered in excreta collected to date, or 2) radioactivity is undetectable in urine and feces during 2 consecutive 24-hour collection periods, or 3) until the end-of-study (EoS) visit on Day 206.

Participants will receive the appropriate containers to collect all feces at home within 24 hours prior to admission on Day -1 and each of the 24-hour stays. This sample will be used if no feces is produced between admission on Day -1 and dosing (as blank sample) or during the 24-hour stays after Day 29, respectively.

The total duration of study participation from screening until EoS visit will be up to approximately 234 days. For an overview of the study design, see Table 1.

Table 1 Schematic Study Design

Visit Activity	Screening	Long-term confinement in CRU			24-hour visits (up to 11 visits) [a]
	Eligibility	Admission	Dosing	Assessments/ PK sampling	PK sampling (collection of blood and excreta)
Study Day(s)	-28 to -2	Day -1	Day 1	Days 1 to 29 (ie, discharge)	35-36 (±1 day), 42-43 (±1 day), 56-57(±2 days), 70-71 (±2 days), 84-85 (±2 days), 98-99 (±2 days), 112-113 (±2 days), 136-137 (±2 days), 150-151 (±2 days), 178-179 (±2 days), 206-207 (±2 days; EoS/ET)

CRU=clinical research unit; EoS=end of study; PK=pharmacokinetic(s)

[a] Criteria for ending the collection of blood and excreta in a participant after Day 29 are: 1) ≥90% of the administered radioactive dose is recovered in excreta collected to date, or 2) radioactivity is undetectable in urine and feces during 2 consecutive 24-hour collection periods, or 3) until the EoS visit on Day 206. If these criteria are met after Day 29 and before Day 206, participants will return to the CRU for EoS assessments at a separate visit 7 (±3) days after the last 24-hour visit.

6.1 Sample Size Considerations

No formal sample size calculation was made. Based on similar studies, the sample size of 8 – 10 participants was considered appropriate for this Phase 1 ADME study.

7.0 Overview of Planned Analysis

7.1 Changes from Protocol

The % Hb occupancy (at C_{max}) was added as a PK parameter.

The protocol states “Concentrations of total radioactivity in blood and excreta will be assayed weekly during the 30-day confinement phase and thereafter within 3 days of the 24-hour collections.” However, blood and plasma will not be assayed weekly for concentrations of total radioactivity during the 30-day confinement phase. Only excreta will be assayed weekly for total radioactivity during the 30-day confinement phase, as described in the Protocol Clarification Memo dated 27-Oct-2022.

The definition of treatment emergent adverse events (TEAEs) has been updated compared to the protocol. TEAE are those which occur (or worsen) after the dose of study drug, consistent with the protocol text. Additionally, AEs need to take place during the on-treatment period, defined as the period after the dose of study drug and before the minimum of (Study Day 56, study discontinuation), to be considered as TEAEs. Day 56 has been chosen for this purpose based on the half-life of GBT021601.

7.2 Planned interim Analysis and Key Results

There are no interim analyses planned for this study.

7.3 Final Analysis

The final TFLs will be created after all participants have completed the end of study (EOS) visit or have discontinued the study.

8.0 Data Review

8.1 Data Management

Data handling and transfer will take place under the ICON Data Management Plan for the study.

8.2 Acceptance of Data for Summarization

Programming of analysis datasets and TFLs may be ongoing during the data management of the study. However, programming of analysis datasets and TFLs will be completed and quality controlled (QC'd) after database lock. The draft safety TFLs will also be QC'd before database lock. Only quality assured (QA'd) results released by the Safety Laboratory, Bioanalytical Laboratory, or other external data source will be used for the programming of analysis datasets and TFLs for the final report. Any data values requiring investigation or corrections that are identified while programming the analysis datasets and TFLs will be sent to the project Data Manager for resolution. If the issue affects the TFLs the Programmer or Statistician who identified the issue will follow it to resolution.

9.0 Definitions and General Analysis Methods

9.1 Analysis Data Presentation

9.1.1 Rounding

In listings, data will be presented with the same precision as the original data. Derived data will be rounded for presentation purposes.

For all summaries, the mean and median will be presented to one decimal place greater than the data, standard deviation to 2 greater than the data, and the minimum (min) and maximum (max) will be presented to the same number of decimal places as the data. Frequency percentages will be presented with one decimal. Individual values and descriptive statistics of PK concentrations in all matrices (e.g. whole blood, plasma) and parameters will generally be presented with 3 decimals, except t_{max} (which will be reported with 2 decimals). Values greater than 999 will be presented as integers. The coefficients of variation (CVs) as a percentage will be presented to 1 decimal place.

9.1.2 Imputation

Unless otherwise noted, data will not be imputed. Imputation will only be used for:

- PK concentrations below the quantifiable limit (BQL) (see Section 16.1.2).
- PK amounts excreted will be interpolated between confinement and 24 hour visits and between subsequent 24 hour visits (see Section 16.1.2)
- Missing start or end date/times of AEs for the calculation of onset and duration (see Section 17.1.1).
- Missing adverse event (AE) severity, relationship and seriousness of AEs see Section 17.1.1).
- Safety laboratory data that are <x or >x (e.g. "<1.03", ">1000"): the analysis value or normal limit value will be the value of the detection limit itself plus or minus one precision unit for the parameter concerned (respectively 1.02 and 1001 in the example). The values before imputation ("<1.03", ">1000") will only be shown in listings. Listings will present the values before imputation.

9.1.3 Descriptive Statistics

Unless otherwise indicated, continuous variables will be summarized with the following descriptive statistics: n (number of observations), (arithmetic) mean, standard deviation (SD), min value, median, and max value. For the summary statistics for PK, see Section 16.2.1 for PK concentrations and Section 16.2.3 for PK parameters.

Categorical data will be summarized with frequencies and percentages. Percentages by categories will be based on the number of participants exposed.

For categorical data, the categories will be presented in the tables exactly as they appear in the CRF / Database.

9.1.4 Pooling

Data will not be pooled.

9.1.5 Unscheduled Measurements

Unscheduled measurements will be included in the listings. With the exception of unscheduled measurements used for baseline, unscheduled measurements will be excluded from the descriptive statistics and statistical analysis.

9.2 Analysis Data Definitions

9.2.1 Baseline Definition

Unless otherwise stated, baseline for postdose evaluations is defined as the last observation recorded before study drug administration. The last observation can be an unscheduled measurement, in which case the baseline can be an unscheduled measurement.

9.2.2 Treatment/Participant Grouping

Label	Grouping
Study Drug	GBT021601 + ^{14}C-GBT021601
Treatment/Dose Level	200 mg GBT021601 + ~74 kBq (~2 µCi) ^{14}C-GBT021601

9.2.3 Common Variable Derivations

Variable	Data Type	Definition/Calculation
Change from Baseline	All	Postdose Observation minus Baseline Observation
Analysis Study Day (Prior to Dose)	All	Date of Measurement minus Dose Date
Analysis Study Day (Post Dose)	All	Date of Measurement minus Dose Date +1
Day 1	All	Day 1 starts at date/time of dosing

9.2.4 ADaM Datasets and Metadata

The analysis datasets will be generated in accordance with Clinical Data Interchange Standard Consortium (CDISC) Analysis Data Model (ADaM) Version 2.1. The ADaM datasets in Table 2 ADaM Datasets will be created, with independent production and validation programming, per ICONs SOP. Additional ADaMs may be created, if needed for TFL programming.

Table 2 ADaM Datasets

ADaM Dataset Name	Description
ADSL	Subject-Level Analysis Dataset
ADAE	Adverse Events Analysis Dataset

ADaM Dataset Name	Description
ADEG	ECG Analysis Dataset
ADLB	Laboratory Test Results Analysis Dataset
ADPC	Pharmacokinetic Concentrations Analysis Dataset
ADPP	Pharmacokinetic Parameters Analysis Dataset
ADVS	Vital Signs Analysis Dataset

ADaM compliant datasets will be delivered to the sponsor. A define.xml file version 2 with the corresponding metadata will be included.

9.3 Software

The statistical analysis and reporting will be done using SAS® for Windows™ Version 9.4 or higher (SAS Institute, Inc.).

PK parameter calculations will primarily be done using Phoenix® WinNonlin® (WNL) Version 8.3.4.295 or higher (Certara USA Inc.). Additional PK computations may be performed in SAS®.

9.4 Statistical Methods

9.4.1 Statistical Outlier Determination

No statistical outlier analysis is planned.

9.4.2 Predetermined Covariates and Prognostic Factors

There are no predetermined covariates or prognostic factors.

9.4.3 Hypothesis Testing

No formal hypothesis testing will be done.

9.5 TFL Layout

Report layout will be according to the ICON EDS – International Conference on Harmonization (ICH) E3 compliant – CSR Template. The layout of TFLs will be according to the ICON EDS standards.

Table shells will be provided as separate document to this SAP. Small changes to TFL layout compared to the shell layout, due to the nature of the data may be required after database lock at the discretion of the ICON project statistician.

The TFLs will be provided in rtf format (one file for the Participant Data Listings, and one for the Table and Figures) referred to, but not included in text.

Format:

- Data in listings will be sorted by participant number and time point.
- Data in tables will be sorted by time point.
- Column titles will be in title case letters.
  All tables and listings will be in landscape format with minimum of 1 inch margin at the top, 3/4" edge margin at the bottom and 1/2" for other margins. All figures will be in portrait format, with the exception of the combined individual plots, which will be in landscape format.
- Courier New of no less than 8-point will be used for tables and listings.
- The treatment labels will be as outlined in Section 9.2.2.

10.0 Analysis Sets

Table 3 Analysis Sets

Analyses	Enrolled Set	Safety Set	Pharmacokinetic Set
Disposition Summaries	✓		
Safety Assessments		✓	
Baseline Characteristics		✓	
PK Concentrations		✓a	✓b
PK Parameters			✓

a: For PK concentration listings. b: For PK concentration summaries.

10.1 Enrolled Set

The enrolled set will consist of all subjects that signed the Informed Consent Form. This set will be used for disposition summaries.

10.2 Safety Set

All participants who have received 1 dose of GBT021601. This set will be used for the safety data summaries, baseline characteristic summaries and PK concentration listings.

10.3 Pharmacokinetic Set

All participants who have received 1 dose of GBT021601 and provided at least 1 measurable postdose PK concentration of GBT021601 or total radioactivity in whole blood or plasma. This set will be used for PK concentrations and PK parameter summaries.

11.0 Participant Disposition

The number and percentage of participants dosed, and members of each analysis set will be presented. The number and percentage of participants who withdrew from the study prematurely and a breakdown of the corresponding reasons for withdrawal will also be presented.

12.0 Protocol Deviations and Violations

Protocol deviations will be listed.

13.0 Demographic and Baseline Characteristics

13.1 Demographics

All demographic data as collected during the screening visit will be listed by participant.

Participant demographics will be summarized descriptively for all participants. The summary will include the participants' age (in years), gender, race, ethnicity, weight (in kg), height (in cm), and body mass index (BMI) (in kg/m^2) measured at screening. Demographics will be summarized for the safety and PK sets, if they are different.

13.2 Medical History

Medical history, categorized by preferred term according to Medical Dictionary for Regulatory Activities (MedDRA) (Version 25.0), will be listed.

13.3 Other Baseline Characteristics

The results of drug and alcohol screen at screening and baseline will be listed.

The results of serology at screening will be listed.

The results of SARS-CoV-2 tests will be listed.

The results of pregnancy tests (beta-human chorionic gonadotropin β-HCG) and follicle stimulating hormone (FSH) test results will be listed.

Non-compliance to in- or exclusion criteria (if any) will be listed.

14.0 Concomitant Medications

Concomitant medications, categorized by medication group and subgroup according to WHO Drug Dictionary (Version WHO Drug Global B3 SEP2022), will be listed.

Medications with an end date prior to the dose of study drug will be considered prior medications and will be noted in the listing. Concomitant medications are defined as those taken by the participant at any time between the date of study drug administration and study completion/discontinuation. Medication with start date being partially or completely missing will be assumed to be concomitant if it cannot be definitively shown that the medication did not occur during treatment. Any ongoing medications, either with a start date before study drug administration or during the study period, will be reported as concomitant medication.

15.0 Treatment Compliance and Exposure

Exposure data will be listed by participant.

A listing of study dates (date of informed consent signature, date of medication, and follow-up) will be provided.

16.0 Pharmacokinetic Analyses

16.1 Pharmacokinetic Variables

PK concentrations will be measured in whole blood, plasma, CCI urine, feces and vomitus (if applicable).

16.1.1 Plasma, Whole Blood and CCI Variables

16.1.1.1 Concentrations

- Plasma concentration of GBT021601
- Whole blood concentration of GBT021601
- CCI
- Plasma concentration of ^{14}C-GBT021601 total radioactivity
- Whole blood concentration of ^{14}C-GBT021601 total radioactivity
- CCI

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[redacted]

16.1.1.2 Whole Blood, Plasma and CCI Parameters

- PK Parameters for GBT021601 and ^{14}C-GBT021601 total radioactivity are defined in Table 4.

Table 4: Whole Blood, Plasma and CCI Parameters

Parameter	Description	Analyte	Matrix
C_{max}	Maximum observed concentration	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
t_{max}	Time to attain maximum observed concentration	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
AUC_{0-24}	Area under the plasma concentration-time curve up to 24 hours postdose	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
AUC_{0-t}	Area under the plasma concentration-time curve up to time t, where t is the last point with concentrations above the lower limit of quantification	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
AUC_{0-inf}	Area under the plasma concentration-time curve from time 0 to infinity calculated as: $AUC_{0-inf}=AUC_{0-t}+C_{last}/k_{el}$, where C_{last} is the last measurable plasma concentration	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
K_{el} (also denoted as λ_z)	Apparent terminal phase rate constant calculated by linear regression of the terminal log-linear portion of the concentration vs. time curve. Linear regression of at least three points and adjusted R^2 greater than 0.80 are required to obtain a reliable λ_z.	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
$t_{1/2}$	Terminal phase half-life expressed in time units. Adjusted R^2 greater than 0.80 is required to obtain a reliable $t_{1/2}$. If adjusted $R^2 \leq .80$ then parameter is not included	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
CL/F	Apparent total clearance, calculated as dose/AUC_{0-inf}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
V_z/F	Apparent volume of distribution at terminal phase, calculated as: $(CL/F)/K_{el}$	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
Ratio AUC B:P	Blood to plasma ratio based on AUC_{0-inf}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma
Ratio C_{max} B:P	Blood to plasma ratio based on C_{max}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma
[redacted]	CCI [redacted]	[redacted]	[redacted]

Parameter	Description	Analyte	Matrix
[redacted]	CCI [redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
%AUCextrap	Percentage of $AUC_{0\text{-}inf}$ that is due to extrapolation from the time of last observed concentration to infinity.	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
Adj R^2	Goodness of fit statistic for the loglinear terminal elimination phase of the concentration time profile identified by least squares linear regression and adjusted for the number of points (minimum of 3) used in the estimation of K_{el}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
K_{el}_Start	The start time used in the regression for the determination of K_{el}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
K_{el}_End	The end time used in the regression for the determination of K_{el}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI
K_{el}_N	The number of points used in the regression for the determination of K_{el}	^{14}C-GBT021601 Total Radioactivity, GBT021601	Whole Blood, Plasma, CCI

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Note: AUCs will be calculated using the linear/log trapezoid rule, expressed in units of concentration x time. Additional PK parameters may be generated at the discretion of the PK specialist or the sponsor.

16.1.2 Urine, Feces and Vomitus (if applicable) Variables

16.1.2.1 Concentrations

- GBT021601 concentrations and amounts excreted in urine and feces
- ^{14}C-GBT021601 Total Radioactivity, concentrations and amounts excreted in urine
- ^{14}C-GBT021601 Total Radioactivity, concentrations and amounts excreted in feces
- ^{14}C-GBT021601 Total Radioactivity, concentrations and amounts excreted in vomitus, if applicable.

16.1.2.2 Pharmacokinetic Amounts Excreted

Urinary and fecal PK parameters will be calculated using SAS and/or WNL. Excretions in mg equivalent (mg eq) for each interval ($Ae_{t1\text{-}t2}$) will be derived from the urinary and fecal concentrations and the sample collection interval volumes or weights respectively, by multiplying the concentration in the interval (C) and the volume or weight (V):

$$Ae_{t1-t2} = C \times V$$

If the concentration is < lower limit of quantification (LLOQ), the excretion will be assumed to be zero. For intervals in which no sample was collected (e.g., no defecation), the excretion will be assumed to be zero.

Cumulative excretions for each continuously sampled interval will be calculated by adding the excretions in the current and all previous collection intervals:

$$Ae_{0-t} = \sum_{i=1}^{n} \left(Ae_{t_{start}-t_{end}}\right)_i$$

The excretion rate ($\Delta Ae/\Delta t$) will also be calculated by dividing the excretion in each interval by the time difference in hours between the end and the start of the collection interval:

$$\frac{\Delta Ae}{\Delta t} = \frac{Ae}{t_{end} - t_{start}}$$

If a participant has not met the criteria for ending the collection of blood and excreta on Day 29 (i.e., end of confinement), cumulative excretion will be calculated up to and including the last continuous 24 hour visit during confinement. Interpolation will be used to estimate urinary and fecal excretion between confinement and 24 hour visits and between subsequent 24 hour visits, the midpoint method will be used to estimate Ae t_{start}-t_{end}. The excretion rate of each collection interval will be plotted as a function of the midpoint of the respective interval. The area under this curve is Ae.

16.1.2.3 Excretion Parameters

- PK Parameters for GBT021601 and ^{14}C-GBT021601 total radioactivity as defined in Table 5.

Table 5 PK parameters for excretion

Parameter	Description	Analyte
CL_R	Renal clearance	GBT021601
Ae_{urine}	Cumulative amount of drug excreted in urine at each interval	^{14}C-GBT021601 Total Radioactivity, GBT021601
fe_{urine}	Fraction of the dose administered excreted in urine (%) at each interval	^{14}C-GBT021601 Total Radioactivity, GBT021601
Ae_{feces}	Cumulative amount of drug excreted in feces at each interval	^{14}C-GBT021601 Total Radioactivity
fe_{feces}	Fraction of the dose administered excreted in feces (%) at each interval	^{14}C-GBT021601 Total Radioactivity
Ae_{vomit}	Cumulative amount of drug excreted in vomitus (if applicable)	^{14}C-GBT021601 Total Radioactivity
fe_{vomit}	Fraction of the dose administered excreted in vomitus (%), if produced	^{14}C-GBT021601 Total Radioactivity
Ae_{total}	Total amount of drug excreted in urine and feces	^{14}C-GBT021601 Total Radioactivity
fe_{total}	Total fraction of the dose administered excreted in urine and feces	^{14}C-GBT021601 Total Radioactivity

The administered dose is calculated by multiplying the amount (400 mL) of the solution given by the radioactivity per mL of the solution.

The radioactivity per mL solution is calculated by multiplying the label claim (0.185 kBq/mL) by the % radioactivity results (98.5%) of the product (which is established by the QC department):

$$Administered\ dose = 400\ mL * 0.185\ (kBq/mL)\ *\ 0.985\ =\ 72.89\ kBq$$

16.2 Pharmacokinetic Summaries

16.2.1 Pharmacokinetic Concentrations

Individual whole blood, plasma and CCI concentration data will be presented together with descriptive statistics by time point for each analyte. Participants excluded from the PK analysis set will be flagged.

Whole blood, plasma and CCI concentrations that are BQL will be set to zero in the computation of descriptive statistics of concentration values. Descriptive statistics (number of subjects, arithmetic mean, geometric mean, standard deviation (StDev), coefficient of variation, geometric coefficient of variation, median, min, and max) will be used to summarize the whole blood, plasma and CCI concentrations at each scheduled time point. If over two thirds of the participants at a specific time point have values BQL then the descriptive statistics will not be presented, with the exception of n, min (<LLOQ) and max.

Linear and semi-logarithmic plots of the arithmetic mean with error bars whole blood, plasma and CCI concentrations by scheduled sampling time will be provided. These plots are planned to show time in days, but might be adjusted to another time unit based on the data. The plots will match the summary table results and will not have an observation at a given time point if more than two thirds of the participants have values BQL.

Linear and semi-logarithmic plots of the individual whole blood, plasma and CCI concentration by actual sampling time will be provided by participant. These plots will show time in hours. Individual plots will use the BQL handling procedure described below for Pharmacokinetic Parameters.

Linear and semi-logarithmic spaghetti plots of the (combined) individual whole blood, plasma and CCI concentrations by actual sampling times will be provided. The full profile of the treatment will be presented in one plot. These plots will show time in hours. Spaghetti plots will use the BQL handling procedure described below for Pharmacokinetic Parameters.

Time deviations from planned dosing (only those not equal to zero) and comments will be listed.

16.2.2 Whole Blood CCI to Plasma Ratios

Individual values of the ratios will be presented together with descriptive statistics by time point for the ratio of CCI to whole blood or plasma for ^{14}C-GBT021601 Total Radioactivity

16.2.3 Pharmacokinetic Parameters

PK parameters will be estimated using non-compartmental methods with WinNonlin® and additional computations may be performed in SAS.

The whole blood, plasma and CCI for GBT021601 and ^{14}C-GBT021601 Total Radioactivity will be estimated from the concentration-time profiles. In estimating the PK parameters, BQL values at the beginning of the profile will be set to zero. BQL values that occur after the first quantifiable point will be considered missing. Values that are embedded between BQLs, or quantifiable values occurring after 2 or more BQLs, will be set to missing at the discretion of the pharmacokineticist. All concentration values reported as no results (not collected or not determined (ND)) values will be treated as missing. Actual sampling times, rather than scheduled sampling times, will be used in all computations involving sampling times.

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Descriptive statistics (number of participants, mean, geometric mean, standard deviation, coefficient of variation, geometric coefficient of variation, median, minimum, and maximum) will be used to summarize the calculated PK parameters for GBT021601 and Total Radioactivity. For ^{14}C-GBT021601 Individual plasma PK parameters will be presented together with descriptive statistics. For t_{max}, only median, min and max will be presented.

Only data points that describe the terminal elimination log-linear decline will be used in the regression equation for calculation of λ_z; C_{max} and any data point in the distribution phase are not included in the calculation. A minimum of 3 points will be used for determination of K_{el}. A general rule of adjusted $R^2 \geq 0.80$ will be considered as acceptable for calculation of K_{el}. If adjusted R^2 falls below 0.80, then λ_z will be reported as Not Determined (ND) and that participant's K_{el}, $t_{1/2}$, CL/F, V_z/F and $AUC_{0\text{-inf}}$ will be reported in the appropriate listings but will be flagged and excluded from descriptive summaries and statistical analysis.

16.2.4 Pharmacokinetic Amounts Excreted

Individual excretion values will be presented together with descriptive statistics by interval and for each analyte and matrix (ie, urine, feces and total).

Descriptive statistics (number of participants, arithmetic mean, geometric mean, standard deviation, coefficient of variation, median, min, and max) will be used to summarize the amounts excreted for GBT021601 and ^{14}C-GBT021601 at each scheduled time interval.

The arithmetic mean values of the cumulative amount excreted in % of the dose in urine, feces and total (urine + feces) versus time (last time point of the interval) will be presented.

Individual plots showing the cumulative amount excreted in % of the dose for all participants versus time (last time point of the interval) in urine, feces and total will be presented.

17.0 Safety Analyses

17.1 Safety Variables

The following safety variables will be summarized:

- Adverse Events (AEs)
- Vital Signs
  - Supine Blood Pressure
    - Systolic Blood Pressure (SBP)
    - Diastolic Blood Pressure (DBP)
  - Heart rate
  - Body temperature
  - Respiration rate
- Electrocardiograms (ECG)
  - Heart Rate
  - PR Interval
  - QRS Duration
  - QT Interval
  - QTcF (Fridericia) Interval
- Clinical Laboratory Evaluations
  - Clinical Chemistry
  - Hematology
  - Urinalysis
  - Coagulation
- Physical Examination

17.1.1 Adverse Events

All AE summaries will include only treatment emergent adverse events (TEAEs). TEAE are those which occur (or worsen) after the dose of study drug during the on-treatment period, defined as the period after the dose of study drug and before the minimum of (Study Day 56, study discontinuation). Day 56 has been chosen for this purpose based on the half-life of GBT021601. All AEs (including non-treatment-emergent events) recorded on the eCRF will be listed, where non-TEAEs will be flagged.

A summary (overview) table with numbers, events and percentages of participants reporting TEAEs, TEAEs related to study drug (related/unrelated), TEAEs by severity (mild, moderate, severe, life-threatening, or death), serious AEs (SAEs), and participants who discontinued the study due to an AE will be provided.

A breakdown of the number of TEAEs, number and percentage of participants reporting each TEAE, categorized by body system and preferred term coded according to MedDRA (Version 25.0), will be presented. Counting will be done by participant (participants will be counted once within each body system or preferred term) and by event.

One such table will be presented for all TEAEs. Another table like this will be presented for TEAEs considered to be related to the study medication. TEAEs' relationship to study drug is categorized as 'related' or 'not related'.

Lastly, one such table for all TEAES by severity (categories as recorded in the eCRF: Grade 1 mild, Grade 2 moderate, Grade 3 severe, Grade 4 life-threatening, or Grade 5 death), will be provided.

A listing of AEs leading to study discontinuation will be provided.

The following missing data will be imputed as defined (will not be presented in listings):

- Missing AE start and / or end times for the calculation of onset and duration will be assumed to be at 00:01 for a start time and 23:59 for end times
- Missing AE severity or relationship will be assumed to be severe or related, respectively
- Missing AE start date/times for the determination of treatment emergence will be assumed to occur during on-treatment period unless partial date/time documents the AE as happening prior to treatment

17.1.2 Deaths and Serious Adverse Events

A listing of deaths and a listing of all SAEs will be provided by participant.

17.1.3 Laboratory Data

Clinical laboratory data will be presented using units from the study data tabulation model (SDTM) Controlled Terminology.

All laboratory data will be listed. A separate listing of out-of-range values will also be provided. Normal ranges will be used directly from the clinical laboratory.

Clinical laboratory results outside the reference range will be flagged. In case the out of reference range values were considered clinically significant by the Investigator, this will also be indicated in the listings as well as in the AE listing. Comments with regard to the laboratory test results will be shown in a separate listing.

Results of continuous parameters recorded as being below or above a detection limit (e.g. “<1.5”, “>800”) will be imputed in the calculation of descriptive statistics as the detection limit plus or minus one precision unit of the respective parameter (in the above example: 1.4 and 801). Listings will present the values before imputation.

Descriptive statistics summarizing continuous laboratory results of clinical chemistry, hematology (observed and derived changes from baseline) and coagulation (observed) by scheduled time will be included.

17.1.4 Vital Signs

All vital signs parameters (including changes from baseline) will be listed by participant. Descriptive statistics will be provided to summarize vital signs (observed and changes from baseline) by scheduled time.

17.1.5 Electrocardiograms

The observed measurements for all ECG parameters and the corresponding abnormalities and physicians’ conclusions will be listed by participant. The means of triplicate measurements for continuous parameters (at screening only) and the change from baseline of the mean triplicate measurements at each scheduled timepoint will be listed by participant.

Descriptive statistics will be provided to summarize mean ECG parameters (observed and changes from baseline) by scheduled time.

17.1.6 Physical Examination

Findings at the physical examination will be listed.

18.0 References

SAS Institute, Inc., SAS® Version 9.4 software, Cary, NC.

Phoenix WinNonlin(R) version 8.1 (Certara USA, Inc. Princeton, NJ, USA)

Clinical Study Protocol. A PHASE 1 STUDY TO ASSESS THE MASS BALANCE, EXCRETION, AND PHARMACOKINETICS OF [^{14}C]-GBT021601, AN ORAL HEMOGLOBIN S POLYMERIZATION INHIBITOR, IN HEALTHY PARTICIPANTS. Version 3.0, Final, 13 Mar 2023.

Appendix 1: Glossary of Abbreviations

Glossary of Abbreviations:	
AE	adverse event
ADaM	analysis data model
ADME	absorption, distribution, metabolism, and excretion
BMI	body mass index
BQL	below the quantifiable limit
CDISC	Clinical Data Interchange Standard Consortium
CRU	Clinical Research Unit
CSR	clinical study report
CV	coefficient of variation
ECG	electrocardiogram
eCRF	electronic case report form
EDS	Early Development Services
EoS	end of study
ICH	International Council for Harmonisation
LLOQ	lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
Max	Maximum
ND	not determined
PK	pharmacokinetic
QA'd	quality assured
QC'd	quality controlled
CCI	[redacted]
SAP	statistical analysis plan
SAE	serious adverse event
sd	Single Dose
StDev	standard deviation
SDTM	study data tabulation model
TEAE	treatment-emergent adverse event
TFL(s)	tables, figures and listings
WHO-DDE	World Health Organization – Drug Dictionary Enhanced
WNL	WinNonlin

Appendix 2: Schedule of Assessments

Study Days / Assessments	Screening (-28 to -2)	Long-term Confinement in CRU (Days -1 to 29) [a]													24-hour Visits [a, b]										
		-1	1	2	3	4	5	6	7	8	14	21	28	29	35 -36	42 -43	56 -57	70 -71	84 -85	98 -99	112 -113	136 -137	150 -151	178 -179	206-207 [EoS/ET]
Long-term confinement		X----------												----X											
Confinement for 24 hours [a]															X	X	X	X	X	X	X	X	X	X	X
Window for 24-hour visits															±1 day		±2 days								
Informed consent	X																								
Demographics	X																								
Medical and surgical history	X	X [c]																							
Review inclusion/exclusion criteria	X	X																							
Height/body weight/BMI [d]	X	X																							
Vital signs [e]	X		X	X											X				X						X [b]
12-lead ECGs [f]	X	X	X																						
Physical examination [g]	X	X																							X [b]
Pregnancy test (females only) [h]	X	X																X		X		X		X	X [b]
FSH test (females only)	X																								
Clinical safety laboratory [i]	X	X							X				X						X						X [b]
Coagulation panel (PT, aPTT, INR)	X																								
Creatinine clearance [j]	X																								
Serology (hepatitis A/B/C, HIV)	X																								
COVID-19 testing (PCR)		X		X											X[r]	X[r]	X[r]	X[r]	X[r]	X[r]	X[r]	X[r]	X[r]	X[r]	X [b, r]
Drug and alcohol screening	X	X													X----------				at indication only						----X [b]
Study drug administration			X																						
CCI [redacted]			[redacted]																						
Blood sampling for PK of GBT021601 and total radioactivity [l]			X	X	X	X	X		X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
CCI [redacted]			[redacted]										[redacted]												
Blood sampling for metabolite identification [n]			X	X	X	X	X	X	X	X	X	X	X						X	X	X	X	X	X	X
Collection of urine [o]			X	X	24-hour collection intervals										X	X	X	X	X	X	X	X	X	X	X
Collection of feces [p]		X	24-hour collection intervals												X	X	X	X	X	X	X	X	X	X	X
Collection of vomitus, if produced [q]			X																						

Previous/concomitant medication	X	X	X----------X [b]
Adverse events	X	X	X----------X [b]

Abbreviations: aPTT=activated partial thromboplastin time; BMI=body mass index; COVID-19=coronavirus disease 2019; CRU=clinical research unit; ECG=electrocardiogram; EoS=end of study; ET=early termination; FSH=follicle stimulating hormone; HIV=human immunodeficiency virus; INR=international normalized ratio; PCR=polymerase chain reaction; PK=pharmacokinetic(s); PT=prothrombin time

a. Participants will be confined in the CRU from Day -1 to 29. Thereafter, participants will return to the CRU for up to 11 visits of 24 hours each to collect whole blood, plasma, urine, and feces. Criteria for ending the collection of blood and excreta in a participant after Day 29 are: 1) ≥90% of the administered radioactive dose is recovered in excreta collected to date, or 2) radioactivity is undetectable in urine and feces during 2 consecutive a 24-hour collection periods, or 3) until the last visit on Day 206.
b. If the criteria for ending the collection of blood and excreta are met after Day 29 and before Day 206, participants will return to the CRU at a separate visit 7 (±3) days after the last 24-hour visit to perform the EoS assessments as indicated with a 'b' in the column for Day 206/207 (EoS/ET).
c. Any updates to medical and surgical history will be recorded.
d. Height will be performed at screening only. BMI will be calculated using the height obtained at screening.
e. Vital signs (heart rate, blood pressure, respiratory rate, and body temperature) will be measured after a participant has rested at least 5 minutes in the supine position. Vital signs will be measured at screening, predose on Day 1, and at 1, 2, 8, 12, and 24 hours postdose, and on Days 35, 84, and 206 (EoS/ET).
f. 12-lead ECGs will be recorded after a participant has rested at least 5 minutes in the supine position. Triplicate ECGs will be recorded at screening only; thereafter, standard single 12-lead ECGs will be taken on Day -1 and on Day 1 at predose and at 1 and 2 hours postdose.
g. A complete physical examination will be conducted at screening. Targeted physical examinations will be conducted at the other time points. Symptom directed physical examinations may also be conducted at any time, per the Investigator's discretion.
h. For females only: serum pregnancy test is required at screening only; urine pregnancy test at all other visits, with serum confirmation if positive.
i. Clinical safety laboratory (including hematology, serum chemistry, and urinalysis) will be obtained at screening and on Days -1, 7, 28, 84, and 206 (EoS/ET).
j. Creatinine clearance (CL_{cr}) will be calculated at screening using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.
CCI [redacted]
l. Whole blood and plasma samples for PK of GBT021601 and total radioactivity will be taken at predose (within 60 minutes prior to GBT021601 dosing), and at 0.25, 0.5, 1, 2, 3, 4, 6, 8, 12, 24 (Day 2), 48 (Day 3), 72 (Day 4), 96 (Day 5), 144 (Day 7), 168 (Day 8), 312 (Day 14), 480 (Day 21), and 648 hours (Day 28) postdose. Additional samples will be obtained on Days 35, 42, 56, 70, 84, 98, 112, 136, 150, 178, and 206 (depending on if criteria for ending collection of urine and feces are met see Footnote a, collection of samples may be ended prior to Day 206). Collections up to and including the 8 hours postdose sample will be collected after a participant has rested at least 5 minutes in the supine position.CCI [redacted]
CCI [redacted]
n. Whole blood and plasma samples for metabolite identification will be collected at predose and 1, 2, 8, 12, 24 (Day 2), 48 (Day 3), 72 (Day 4), 96 (Day 5), 120 (Day 6), 144 (Day 7), 168 (Day 8), 312 (Day 14), 480 (Day 21), and 648 hours (Day 28) hours postdose. Collections up to and including the 8 hours postdose sample will be collected after a participant has rested at least 5 minutes in the supine position. Whole blood and plasma samples for metabolite identification will also be collected at the visits on Days 84 (1992 hours postdose), 98 (2328 hours), 112 (2664 hours), 136 (3240 hours), 150 (3576 hours), 178 (4248 hours), and 206 (4920 hours; EoS/ET).

o. Urine samples for PK of GBT021601 and total radioactivity will be collected on Day 1 (prior to dosing) and after dosing from 0 to 6 hours, 6 to 12 hours, 12 to 24 hours postdose, and thereafter in 24-hour intervals up to Day 29. Urine will also be collected in 24-hour intervals starting on Days 35 (816 hours postdose), 42 (984 hours), 56 (1320 hours), 70 (1656 hours), 84 (1992 hours), 98 (2328 hours), 112 (2664 hours), 136 (3240 hours), 150 (3576 hours), 178 (4248 hours), and 206 (4920 hours) in accordance with the applicable time windows (depending on if criteria for ending collection of blood and excreta are met see Footnote a, the collection may be ended prior to Day 206). Selected pooled urine will be used for metabolite identification.

p. Fecal collections for the analysis of total radioactivity will be made at predose on Day -1, and complete collections will be made after dosing in 24-hour intervals up to Day 29. Feces will also be collected in 24-hour intervals starting on Days 35 (816 hours postdose), 42 (984 hours), 56 (1320 hours), 70 (1656 hours), 84 (1992 hours), 98 (2328 hours), 112 (2664 hours), 136 (3240 hours), 150 (3576 hours), 178 (4248 hours), and 206 (4920 hours) in accordance with the applicable time windows (depending on if criteria for ending collection of blood and excreta are met see Footnote a, the collection may be ended prior to Day 206). Participants will receive the appropriate containers to collect all feces at home within 24 hours prior to admission on Day -1 and each of the 24-hour stays. These fecal samples will be used if no feces is produced between admission on Day -1 and study drug administration (as a blank sample) or during the 24-hour stays after Day 29, respectively. Selected pooled fecal samples will be used for metabolite identification.

q. Collection of vomitus for analysis of total radioactivity concentrations (if possible), if produced between dosing and 24 hours postdose.

r. COVID-19 testing may be performed at the Investigator's discretion.

Appendix 3: List of End of Text Outputs

List of End of Text Tables and Figures:		
Output	**Title**	**Population Set**
Section 14.1 – Disposition and Demographic Data		
Table 14.1.1	Summary of Participant Disposition	Safety
Table 14.1.2.1	Summary of Demographics – Safety Set	Safety
Table 14.1.2.2	Summary of Demographics – PK Set	PK
Summary of Demographics for the PK set will only be shown if different from the Safety Set		
Section 14.2 – Pharmacokinetic Data		
Section 14.2.1 – Whole Blood, Plasma and CCI		
Table 14.2.1.1	Individual Values and Descriptive Statistics of GBT021601 in Whole Blood, Plasma and CCI Concentrations by Time-Point	PK
Table 14.2.1.2	Individual Values and Descriptive Statistics of ^{14}C-GBT021601 Total Radioactivity in Whole Blood, Plasma and CCI Concentrations by Time-Point	PK
Table 14.2.1.3	Individual Values and Descriptive Statistics of GBT021601 Whole Blood, Plasma and CCI Parameters	PK
Table 14.2.1.4	Individual Values and Descriptive Statistics of ^{14}C-GBT021601 Total Radioactivity Whole Blood and Plasma	PK
Table 14.2.1.5	Individual Values and Descriptive Statistics of %Hb occupancy	PK
Figure 14.2.1.6	Arithmetic Mean Concentrations-Time Profiles of GBT021601 in Whole Blood, Plasma and CCI (Linear and Semi-Logarithmic Scale)	PK
Figure 14.2.1.7	Arithmetic Mean Concentrations-Time Profiles of ^{14}C-GBT021601 Total Radioactivity in Whole Blood, Plasma (Linear and Semi-Logarithmic Scale)	PK
Figure 14.2.1.8	Arithmetic Mean Concentrations-Time Profiles of GBT021601 and ^{14}C-GBT021601 Total Radioactivity in Plasma (Linear and Semi- Scale)	PK
Figure 14.2.1.9	Arithmetic Mean Concentrations-Time Profiles of GBT021601 and ^{14}C-GBT021601 Total Radioactivity in Whole Blood (Linear and Semi-Scale)	PK
Figure 14.2.1.10	Combined Individual Concentrations-Time Profiles of GBT021601 and ^{14}C-GBT021601 Total Radioactivity in Whole Blood, Plasma and CCI by Analyte and Matrix (Linear and Semi-Logarithmic Scale)	Safety
Figure 14.2.1.11	Individual Concentrations-Time Profiles of GBT021601 in Whole Blood, Plasma and CCI	Safety

	and of ^{14}C-GBT021601 Total Radioactivity in Whole Blood and Plasma by Participant (Linear and Semi-Logarithmic Scale)	
Section 14.2.2 – Mass Balance		
Table 14.2.2.1	Individual Values and Descriptive Statistics of Amounts of GBT021601 Excreted in Urine by Interval	PK
Table 14.2.2.2	Individual Values and Descriptive Statistics of Amounts of Total ^{14}C-GBT021601 Radioactivity Excreted in Urine, Feces and Total by Interval	PK
Table 14.2.2.3	Individual Values and Descriptive Statistics of GBT021601 Excretion Parameters in Urine	PK
Table 14.2.2.4	Individual Values and Descriptive Statistics of Total ^{14}C-GBT021601 Radioactivity Excretion Parameters in Urine, Feces and Total Recovery	PK
Figure 14.2.2.5	Arithmetic Mean Cumulative^{14}C-GBT021601 Recovery in Urine, Feces and Total Versus Time	PK
Figure 14.2.2.6	Individual Cumulative ^{14}C-GBT021601 Recovery in Urine, Feces and Total Versus Time	PK
Section 14.3 – Safety Data		
14.3.1 Adverse Events		
Table 14.3.1.1	Overview of Treatment-Emergent Adverse Events	Safety
Table 14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety
Table 14.3.1.3	Summary of Related TEAEs by System Organ Class and Preferred Term	Safety
Table 14.3.1.4	Summary of Treatment Emergent Adverse Events by Severity and Relatedness	Safety
14.3.2 Listing of Deaths and Other Serious Adverse Events		
Table 14.3.2.1	Deaths	All Participants
Table 14.3.2.2	Serious Adverse Events	All Participants
14.3.3 Narratives of Adverse Events Leading to Discontinuation From the Study		
Table 14.3.3	Not part of TFL – Reserved for Narratives in CSR	
14.3.4 Clinical Laboratory		
Table 14.3.4.1	Listing of Out-of-Range Laboratory Values	Safety
Table 14.3.4.2	Summary of Clinical Laboratory Results – Clinical Chemistry	Safety
Table 14.3.4.3	Summary of Clinical Laboratory Results – Hematology	Safety
Table 14.3.4.4	Summary of Clinical Laboratory Results – Coagulation	Safety

14.3.5 Other Safety Parameters		
Table 14.3.5.1	Summary of Vital Signs	Safety
Table 14.3.5.2	Summary of 12-Lead Electrocardiogram	Safety

List of End of Text Listings:	
Output	**Title**
Section 16.2.1 – Disposition	
Listing 16.2.1.1	Participant Disposition
Section 16.2.2 – Protocol Deviations	
Listing 16.2.2.1	Protocol Deviations
Section 16.2.3 – Excluded Participants	
Listing 16.2.3.1	Analysis Sets
Section 16.2.4 – Demographics and Baseline Characteristics	
Listing 16.2.4.1	Participant Demographics
Listing 16.2.4.2	Medical and Surgical History
Listing 16.2.4.3	Prior and Concomitant Medications
Listing 16.2.4.4	Drug and Alcohol Screen
Listing 16.2.4.5	Serology
Listing 16.2.4.6	Pregnancy test
Listing 16.2.4.7	Non-compliance to Inclusion or Exclusion Criteria
Listing 16.2.4.8	SARS-CoV-2 Results
Section 16.2.5 - Compliance	
Listing 16.2.5.1	Study Dates
Listing 16.2.5.2	Study Drug Administration
Section 16.2.6 – Response Data	
Listing 16.2.6.1	Individual Concentrations of GBT021601 and ^{14}C-Radioactivity in Whole Blood, Plasma, and CCI Sampling Time Deviations and Comments
Listing 16.2.6.2	Individual Total Radioactivity Excretion Data in Urine, Feces and Vomitus, Including Volumes, Weights and Amount Excreted
Listing 16.2.6.3	Individual GBT021601 and ^{14}C-Radioactivity Plasma, Whole Blood and CCI Parameters
Section 16.2.7 – Adverse Events Data	
Listing 16.2.7.1	Adverse Events
Listing 16.2.7.2	Adverse Events Leading to Study Discontinuation
Section 16.2.8 – Laboratory Data	

Listing 16.2.8.1	Clinical Laboratory Results – Hematology
Listing 16.2.8.2	Clinical Laboratory Results – Chemistry
Listing 16.2.8.3	Clinical Laboratory Results – Urinalysis
Listing 16.2.8.4	Clinical Laboratory Results – Coagulation
Listing 16.2.8.5	Clinical Laboratory Results – Comments
Section 16.2.9 – Other Safety Data	
Listing 16.2.9.1	Vital Signs
Listing 16.2.9.2	12-Lead Electrocardiogram Results
Listing 16.2.9.3	Physical Examination
Listing 16.2.9.4	Body Weight

Appendix 4: Shells for Post-Text Tables, Figures and Listings

Shells are provided in a separate document.

19.0 Document History

Version Date	Modified/Reviewed By	Brief Summary of Changes (if created from a template, include template code)
09-Feb-2023	PPD	Initial version
21-Feb-2023		Updated after internal review
15-March-2023		Updated after sponsor review
06-Apr-2023		Updated after further sponsor review
25-Apr-2023		Updated after review of sponsor QC statistician
01-May-2023		Updated after further review of sponsor QC statistician