TransCelerate BIOPHARMA INC.

Common CSR Template Mapped to ICH E3 and CORE Guidance

ICH E3	CORE	Common CSR	Rationale
1. TITLE PAGE	1. TITLE PAGE	TITLE PAGE	Per CORE, title page does not require a Heading number. First 5 sections are unnumbered as: - no longer needed for navigation - numbering will be disrupted when some sections are deleted from full CSR template to create abbreviated or synoptic CSRs in future release
2. SYNOPSIS	2. SYNOPSIS	SYNOPSIS	
3. TABLE of Contents	3. TABLE of Contents	TABLE OF CONTENTS	
4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS	4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS	LIST OF ABBREVIATIONS AND DEFINITION OF TERMS	
5. ETHICS	5. ETHICS	ETHICS	
5.1 INDEPENDENT ETHICS COMMITTEE AND/OR INSTITUTIONAL REVIEW BOARD	5.1 INDEPENDENT ETHICS COMMITTEE AND/OR INSTITUTIONAL REVIEW BOARD	INDEPENDENT ETHICS COMMITTEE AND/OR INSTITUTIONAL REVIEW BOARD	Subheadings are unnumbered in alignment with first 5 Level 1 sections.
5.2 ETHICAL CONDUCT OF THE STUDY	5.2 ETHICAL CONDUCT OF THE STUDY	ETHICAL CONDUCT OF THE STUDY	
5.3 SUBJECT INFORMATION AND CONSENT	5.3 SUBJECT INFORMATION AND CONSENT	SUBJECT INFORMATION AND CONSENT	
6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE	6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE	-	Section moved to Section 3.2 as related to the Investigational Plan information.
7. INTRODUCTION	7. INTRODUCTION	1. INTRODUCTION	
8. STUDY OBJECTIVES	8. STUDY OBJECTIVES AND ENDPOINTS	2. STUDY OBJECTIVES AND ESTIMANDS [ENDPOINTS]	Estimands are being introduced into CPT in 2018 in accordance with ICH E9 (R1) guidance. The CSR template has been aligned with the CPT, but sponsors may use endpoints if applicable. Note that endpoints are included as part of the estimands.
	8.1 OBJECTIVES	-	The Objectives/Estimands [Endpoints] table will be brought in from the CPT; as both objectives and endpoints are in the same table, there is no need for subsections.
	8.2 ENDPOINTS	-	
9. INVESTIGATIONAL PLAN	9. INVESTIGATIONAL PLAN	3. INVESTIGATIONAL PLAN	

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9.1 OVERALL STUDY DESIGN AND PLAN - DESCRIPTION	**9.1 OVERALL STUDY DESIGN AND PLAN**	**3.1 OVERVIEW OF STUDY DESIGN**	Heading name streamlined for clarity and brevity.
9.2 DISCUSSION OF STUDY DESIGN, INCLUDING THE CHOICE OF CONTROL GROUPS	**9.2 DISCUSSION OF STUDY DESIGN, INCLUDING THE CHOICE OF CONTROL GROUPS**	**3.1.1 Discussion of Study Design**	Heading name streamlined for clarity and brevity.
		3.1.2 Change in Study Conduct	Subsections of ICH E3 and CORE Section 9.8.1 Changes in Conduct of Study or Planned Analyses were moved to group changes in study conduct with the overall study design (Common CSR section 3.1.2) and changes in planned analyses with the statistical analyses section (Common CSR section 3.7.2), respectively.
		3.2 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE	Section moved from Section 6 in ICH E3 and CORE as it is related to the Investigational Plan information.
9.3 SELECTION OF STUDY POPULATION	**9.3 SELECTION OF STUDY POPULATION**	**3.3 SELECTION OF STUDY POPULATION**	
		3.3.1 Eligibility Criteria	To support a streamlined CSR, a high-level summary of eligibility criteria is to be provided here, with reference out to full Inclusion and Exclusion Criteria in the appended protocol.
9.3.1 Inclusion Criteria	**9.3.1 Inclusion Criteria**	**-**	Subsections deleted as described above.
9.3.2 Exclusion Criteria	**9.3.2 Exclusion Criteria**	**-**	
9.3.3 Removal of Patients from Therapy or Assessment	**9.3.3 Removal of Subjects from Therapy or Assessment**	**3.3.2 Removal of Participants From Intervention or Study**	Updated from Subject to Participant to be consistent with CPT, FDA, and NIH. Changed from Assessment to Study for clarity.
	9.3.4 Stopping or Suspending the Study		Describe in Common CSR Section 3.1.2 Changes in Study Conduct

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ICH E3	CORE	Common CSR	Rationale
9.4 TREATMENT	**9.4 TREATMENT**	**3.4 STUDY INTERVENTION**	Updated from Treatment to Study Invention to be consistent with CPT, FDA, and NIH.
9.4.1 Treatment Administered	**9.4.1 Treatment Administered**	**3.4.1 Study Intervention(s) Administered**	All study interventions (investigational or non-investigational) will be provided in this section. In the CPT, these are all described in one table/section. To facilitate reuse from the CPT, a single section is provided here. Directional text and links to the appendix will be provided for batch numbers and individual intervention assignments.
	9.4.1.1 Investigational Product(s)	-	See above
	9.4.1.2 Non-Investigational Product(s)	-	See above
9.4.2 Identity of Investigational Product(s)	**9.4.2 Identity of Investigational Product(s)**	-	Directional text and links to the appendix will be provided for batch numbers in Section 3.4.1.
	9.4.3 Avoidance of Bias	**3.4.2 Measures to Minimize Bias**	
9.4.3 Methods of Assigning Subjects to Treatment Groups	**9.4.3.1 Methods of Assigning Subjects to Treatment Groups**	-	To support a streamlined CSR, directional text and links to the protocol will be provided under Section 3.4.2.
9.4.6 Blinding	**9.4.3.2 Blinding and Unblinding**	-	
9.4.4 Selection of Dose(s) in the Study			Redundant; provided in table above in Section 3.4.1. Directional text and links to the appendix will be provided for individual intervention assignments in Section 3.4.1.
9.4.5 Selection of Timing and Dose(s) for Each Patient	**9.4.4 Selection of Dose(s) and Timing of Dose for Each Subject**	-	
9.4.8 Treatment Compliance	**9.4.5 Treatment Compliance**	**3.4.3 Study Intervention Compliance**	
9.4.7 Prior and Concomitant Therapy	**9.4.6 Prior and Concomitant Therapy**	**3.4.4 Prior, Concomitant, and/or Post-intervention Therapy**	

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ICH E3	CORE	Common CSR	Rationale
9.5 EFFICACY AND SAFETY VARIABLES	**9.5 EFFICACY AND SAFETY VARIABLES**	**3.5 STUDY ASSESSMENTS AND PROCEDURES**	Updated heading to align with CPT.
9.5.1 Efficacy and Safety Measurements Assessed and Flow Chart	**9.5.1 Efficacy and Safety Measurements Assessed and Schedule of Assessments**	**3.5.1 Planned Measurements and Timing of Assessments**	Heading updated for clarity.
9.5.3 Primary Efficacy Variable	**9.5.1.1 Primary Efficacy Measurement**	-	To support a streamlined CSR, directional text and links to the protocol will be provided. Companies may choose to insert subsections if desired.
	9.5.1.2 Secondary Efficacy Measurements	-	
	9.5.1.3 Other Efficacy Measurements	-	
	9.5.1.4 Safety – Adverse Events	-	
	9.5.1.5 Safety – Clinical Laboratory Evaluation	-	
	9.5.1.6 Safety – Vital Sign Measurements	-	
	9.5.1.7 Safety – Physical Examination	-	
9.5.2 Appropriateness of Measurements	**9.5.2 Appropriateness of Measurements**	**3.5.2 Appropriateness of Measurements**	
		3.5.3 Additional Summary of Specific Measurements	Provided to allow more detail around specific assessments if needed.
	9.5.3 Pharmacologic and Pharmacodynamic Measurements	-	To support a streamlined CSR, directional text and links to the protocol will be provided in Section 3.5.1. Companies can choose to insert subsections into Section 3.5.1 or Section 3.5.3 if desired.
9.5.4 Drug Concentration Measurements	**9.5.3.1 Pharmacokinetic Measurements**	-	
	9.5.3.2 Pharmacokinetic Parameters	-	
	9.5.3.3 PD Measurements	-	
	9.5.3.4 PD Parameters	-	
	9.5.4 Other Measurements	-	
9.6 DATA QUALITY ASSURANCE	**9.6 DATA QUALITY ASSURANCE**	**3.6 DATA QUALITY ASSURANCE**	

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ICH E3	CORE	Common CSR	Rationale
9.7 STATISTICAL ANALYSIS METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE	**9.7 STATISTICAL ANALYSIS METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE**	**3.7 STATISTICAL ANALYSIS**	
9.7.1 Statistical and Analytical Plans	**9.7.1 Statistical Plans**	**3.7.1 Statistical Plans**	To support a streamlined CSR, directional text and links to the protocol will be provided for the majority of details for the statistical analyses with the exception of changes in planned analyses and changes following study unblinding or post-hoc analyses that will not have been described in the statistical analysis plan.
	9.7.1.1 General Approaches	**-**	
	9.7.1.2 Primary Efficacy Endpoint Methodology	**-**	
	9.7.1.3 Secondary Efficacy Endpoint Methodology	**-**	
	9.7.1.4 Other Efficacy Endpoint Methodology	**-**	
	9.7.1.5 Safety Endpoint Methodology	**-**	
	9.7.1.6 PK and PD Endpoint Methodology	**-**	
	9.7.1.7 Other Endpoint Methodology	**-**	
9.7.2 Determination of Sample Size	**9.7.2 Determination of Sample Size**		
9.8 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS	**9.8 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS**	**-**	
	9.8.1 Changes in the Conduct of the Study	**-**	Moved to Common CSR Section 3.1.2.
	9.8.2 Changes in the Planned Analyses	**3.7.2 Changes in Planned Analysis**	
	9.8.3 Changes Following Study Unblinding and Post-hoc Analyses	**3.7.3 Changes Following Study Unblinding and Post-hoc Analyses**	
10 PATIENTS	**10 STUDY SUBJECTS**	**4 STUDY PARTICIPANTS**	Terms updated to be consistent with CPT, FDA, and NIH.

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ICH E3	CORE	Common CSR	Rationale
10.1 DISPOSITION OF PATIENTS	**10.1 DISPOSITION OF SUBJECTS**	**4.1 DISPOSITION OF PARTICIPANTS**	Terms updated to be consistent with CPT, FDA, and NIH.
10.2 PROTOCOL DEVIATIONS	**10.2 PROTOCOL DEVIATIONS**	**4.2 PROTOCOL DEVIATIONS**	
11.1 DATA SETS ANALYZED	**10.3 DATA SETS ANALYZED**	**4.3 POPULATIONS ANALYZED**	Heading updated for clarity.
11.2 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS	**10.4 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS**	**4.4 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS**	Streamlined content allowed combination of subsections under the same header to describe same topic and similar content.
	10.4.1 Demography	**-**	
	10.4.2 Baseline Disease Characteristics	**-**	
	10.4.3 Medical History and Concurrent Illnesses	**-**	
	10.4.4 Prior and Concomitant Treatments	**4.5 PRIOR, CONCOMITANT, AND POST-INTERVENTION THERAPY**	Section elevated to Level 2 heading as concomitant medications are measured throughout the study, not only at baseline. Post-intervention therapy added to accommodate participants who have completed the intervention period but continue into long term follow up.
11.3 MEASUREMENTS OF TREATMENT COMPLIANCE	**10.5 MEASUREMENTS OF TREATMENT COMPLIANCE**	**4.6 EXPOSURE AND STUDY INTERVENTION COMPLIANCE**	Exposure is often impacted by treatment compliance and by dose modifications. As such, these 3 topics were grouped together as subheadings under Exposure and Study Intervention Compliance.
		4.6.1 Exposure	
		4.6.2 Measurement of Compliance	
		4.6.3 Dose Modifications	
12.1 EXTENT OF EXPOSURE	**10.6 EXTENT OF EXPOSURE**	**-**	Section combined with Exposure (Section 4.6) as exposure is often impacted by treatment compliance.
11 EFFICACY EVALUATION	**11 EFFICACY AND OTHER EVALUATIONS**	**5. EVALUATION OF RESPONSE TO STUDY INTERVENTION**	Many studies assess not only efficacy but other types of assessments as benefits. Given the current regulatory culture of assessing benefits and risks of an intervention, this section was renamed Benefit Evaluations

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11.4 EFFICACY RESULTS AND TABULATIONS OF INDIVIDUAL PATIENT DATA	**11.1 EFFICACY RESULTS**	**5.1 EFFICACY**	Subsections may be added to the section as needed to address the needs of the study.
11.4.1 Analysis of Efficacy	**11.1.1 Primary Efficacy Endpoint**		
	11.1.2 Secondary Efficacy Endpoints		
	11.1.3 Other Efficacy Endpoints		
	11.1.4 *Post-hoc* Analyses		
		5.3 PHARMACOKINETICS	Sections 5.2 through 5.8 are commonly reported result topics; optional Level 2 headers were added to delineate these section for results.
		5.4 PHARMACODYNAMICS	
		5.5 GENETICS	
		5.6 BIOMARKERS	
		5.7 IMMUNOGENICITY	
		5.8 [HEALTH ECONOMICS] OR [MEDICAL RESOURCE UTILIZATION AND HEALTH ECONOMICS]	
		5.9 [OTHER]	Optional Level 2 header added to offer section for other types of results.
11.4.2 Statistical/Analytical Issues	**11.2 RESULTS OF STATISTICAL ISSUES ENCOUNTERED DURING THE ANALYSIS**		Subheadings in CORE are offered as options, as 1 or more may not apply to any give study. Instructional text for Section 5.9 [Other] provides these same options for this section but without the placeholder subheadings. Instructional text will list out examples that could be used.
11.4.2.1 Adjustments for Covariates	**11.2.1 Adjustments for Covariates**	**-**	
11.4.2.2 Handling of Withdrawals, Discontinuations or Missing Data	**11.2.2 Handling of Withdrawals, Discontinuations or Missing Data**	**-**	
11.4.2.3 Interim Analyses and Data Monitoring	**11.2.3 Interim Analyses and Data Monitoring**	**-**	
11.4.2.4 Multicentre Studies	**11.2.4 Multicentre Studies**	**-**	
11.4.2.5 Multiple Comparison/Multiplicity	**11.2.5 Multiple Comparison/Multiplicity**	**-**	

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11.4.2.6 Use of an "Efficacy Subset" of Subjects	**11.2.6 Use of an "Efficacy Subset" of Subjects**	**-**	
11.4.2.7 Examination of Subgroups	**11.2.7 Examination of Subgroups**	**-**	
11.4.3 Tabulation of Individual Response Data	**11.2.8 Tabulation of Individual Response Data**	**-**	
	11.3 PHARMACOKINETIC, PHARMACODYNAMIC AND OTHER ANALYSES RESULTS	**-**	Provided above in Sections 5.3 and 5.4.
11.4.4 Drug Dose, Drug Concentration, and Relationships to Response	**11.3.1 Drug Dose, Drug Concentration and Relationships to Response**	**-**	Can be provided in Sections 5.3 or 5.4.
11.4.5 Drug-Drug and Drug-Disease Interactions	**11.3.2 Drug-Drug and Drug-Disease Interactions**	**-**	Can be provided in Sections 5.3 or 5.4.
11.4.6 By-Patient Displays	**-**	**-**	
	11.3.3 Other Endpoints	**-**	Can be provided in Sections 5.8.
11.4.7 Efficacy Conclusions	**11.4 EFFICACY RESULTS SUMMARY**	**5.10 SUMMARY OF EVAULATION OF RESPOSNE TO STUDY INTERVENTION**	Header name aligned with that of Section 5.
12. SAFETY EVALUATION	**12. SAFETY EVALUATION**	**5.2. SAFETY EVALUATIONS**	Safety evaluations moved under Section 5 Evaluation of Response to Study Intervention.
12.1 ADVERSE EVENTS	**12.1 ADVERSE EVENTS**	**5.2.1 ADVERSE EVENTS**	
12.1.1 Brief Summary of Adverse Events	**12.1.1 Brief Summary of Adverse Events**	**5.2.1.1 Brief Summary of Adverse Events**	
12.1.2 Display of Adverse Events	**12.1.2 Most Frequently Reported Adverse Events**		Frequency of Adverse Events is included in Analyses of All Adverse Events (Section 5.2.1.2).
12.1.3 Analysis of Adverse Events	**12.1.3 Categorisation of All Adverse Events**	**5.2.1.2 Analyses of All Adverse Events**	
12.2.4 Listing of Adverse Events by Patient	**-**	**-**	

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	12.2 ANALYSIS OF DEATHS, OTHER SERIOUS ADVERSE EVENTS, AND OTHER CLINICALLY MEANINGFUL ADVERSE EVENTS	-	To support lean CSR, superfluous headers have been removed and subsequent sections moved up.
	12.2.1 Deaths, Other Serious Adverse Events, Discontinuations due to Adverse Events and Other Adverse Events of Special Interest	-	
	12.2.1.1 Deaths	**5.2.1.3 Death**	
	12.2.1.2 Other Serious Adverse Events	**5.2.1.4 Serious Adverse Events**	
	12.2.1.3 Discontinuations Due to Adverse Events	**5.2.1.5 Discontinuation and/or Dose Modification Due to Adverse Events**	Modification added to support discussion of dose modifications (increase, decrease, or interruption of dose).
	12.2.1.4 Other Adverse Events of Special Interest	**5.2.1.6 Adverse Events of Special Interest**	
		5.2.1.7 Other Significant Adverse Events	
	12.2.2 Narratives of Deaths, Other Serious Adverse Events, and Certain Other Clinically Meaningful Adverse Events	-	To support lean CSR, the use of in-text narratives is discouraged. Instructional text will indicate that if they are necessary, they may be added to the appropriate section above. Full narratives can be provided in an appendix.
	12.3 CLINICAL LABORATORY EVALUATION	**5.2.2 CLINICAL LABORATORY EVALUATION**	Subsections may be added as necessary to address the needs of each study. Suggested subsections are provided in instructional text.
	12.3.1 Individual Laboratory Measurements by Subject and Abnormal Laboratory Values	-	
	12.3.2 Evaluation of Laboratory Values	-	

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ICH E3	CORE	Common CSR	Rationale
	12.3.2.1 Laboratory Values Over Time	**-**	
	12.3.2.2 Individual Subject Changes in Laboratory Values	**-**	
	12.3.2.3 Individual Clinically Meaningful Laboratory Abnormalities	**-**	
	12.4 VITAL SIGNS, PHYSICAL EXAMINATIONS, AND OTHER OBSERVATIONS RELATED TO SAFETY	**5.2.3 OTHER SAFETY EVALUATIONS**	Streamlined header; optional subsections provided below.
	12.4.1 Vital Signs	**5.2.3.1 Vital Signs**	
		5.2.3.2 Electrocardiograms	Added as optional header as a common assessment.
	12.4.2 Physical Examination Findings	**5.2.3.3 Physical Examination Findings**	
		5.2.3.4 Safety Observations Related to [Medical Device OR Combination Product]	Added as optional header to describe evaluations for device or combination (investigational product plus device) products.
	12.4.3 Other Observations Related to Safety	**5.2.3.5 Other Observations Related to Safety**	
	12.5 SAFETY RESULTS SUMMARY	**5.10 Summary of Evaluation of Response to Study Intervention**	
	13 DISCUSSION AND OVERALL CONCLUSIONS	**6. CONCLUSIONS**	To support a streamlined CSR used primarily to deliver study results and retain discussions for summary documents, this section was reduced to cover Conclusions only. Sponsors may include discussions in this section if warranted.
	13.1 DISCUSSION	**-**	Removed subsection to support streamlined CSR.
	13.2 CONCLUSIONS	**-**	

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		7. REFERENCE LIST	Moved up as the document flows better if references are close to the text.
	14 TABLES AND FIGURES		Tables, Listings, and Figures, and Appendices are not listed in the template as those are typically generated separately from the CSR body and attached during publishing. Guidance for these sections is provided in ICH E3 and CORE.
	14.1 DEMOGRAPHIC DATA		
	14.2 EFFICACY DATA		
	14.3 SAFETY DATA		
	14.3.1 Displays of Adverse Events		
	14.3.2 Listing of Deaths, Other Serious and Clinically Meaningful Adverse Events		
	14.3.3 Narratives of Deaths, Other Serious Adverse Events and Certain Other Clinically Meaningful Adverse Events		
	14.3.4 Data Listings (Each Subject) for Abnormal Clinically Meaningful Laboratory Values, Vital Signs, Physical Examinations and Other Observations Related to Safety		
	14.4 OTHER DATA		
	15 REFERENCE LIST		Moved up to Section 7 to be closer to text.
	16 APPENDICES		
	16.1 STUDY INFORMATION		
	16.2 SUBJECT DATA LISTINGS		

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	16.3 CASE REPORT FORMS		
	16.4 INDIVIDUAL SUBJECT DATA LISTINGS		