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PANACEA THERAPEUTICS, INC.

A biopharma company dedicated to a healthy world.

REGULATORY SUBMISSION

INVESTIGATIONAL NEW DRUG (IND) APPLICATION

21 CFR Part 312 | eCTD Format (ICH M4 / FDA Guidance Rev. 8, Sep 2024)

Submitted via FDA Electronic Submissions Gateway (ESG)

Cromaglutide (OBEGO™)

Internal Code: OBS-2020 | GLP-1 Receptor Agonist | Subcutaneous Injection

Field	Details
IND Number	IND-2018-PT-0042
Submission Date	March 14, 2018
Sponsor	Panacea Therapeutics, Inc.
Regulatory Lead	Aastha Dave, Lead Regulatory Affairs
CFR Reference	21 CFR Part 312
eCTD Standard	ICH eCTD v3.2.2 / v4.0 (FDA Rev. 8, Sep 2024)
Submission Gateway	FDA Electronic Submissions Gateway (ESG)
Proposed Phase	Phase 1 — First-in-Human

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Portfolio Note: Sections labelled **[RA-Authored]** reflect content prepared by the Regulatory Affairs function. Sections labelled **[Other Function]** are summarised at high level only. This submission is formatted in **eCTD format** via the FDA ESG per *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (Revision 8, September 2024). Per Table 1 of that guidance, the eCTD requirement for commercial INDs became effective **May 5, 2018**.

Contents

1. Form FDA 1571 — Investigational New Drug Application

Section Owner: Regulatory Affairs CFR Ref: 21 CFR §312.23(a)(1)

Field	Details
Sponsor Name	Panacea Therapeutics, Inc.
Address	500 BioInnovation Drive, Suite 300, Cambridge, MA 02139
Drug Name	Cromaglutide
Proposed Trade Name	OBEGO™
IND Type	☐ Initial IND ☐ Amendment
Proposed Phase	☐ Phase 1
Proposed Indication	Chronic weight management in adults with obesity (BMI ≥30) or overweight (BMI ≥27) with ≥1 weight-related comorbidity
Route of Administration	Subcutaneous injection
Dosage Form	Single-dose pre-filled syringe
Strengths	2.5 mg, 5 mg, 10 mg per 0.5 mL
IND Exempt?	☐ Yes ☐ No
Authorized Signature	Aastha Dave, Lead Regulatory Affairs
Date	March 14, 2018

Commitment Statement (21 CFR §312.23(a)(1)): Panacea Therapeutics, Inc. commits that an IRB complying with 21 CFR Part 56 will be responsible for initial and continuing review and approval of the proposed clinical investigation, and that informed consent will be obtained from each human subject per 21 CFR Part 50.

2. Cover Letter

Section Owner: Regulatory Affairs

Date: March 14, 2018
To: CDER, U.S. Food and Drug Administration
From: Aastha Dave, Lead Regulatory Affairs, Panacea Therapeutics, Inc.
Re: Initial IND Submission — Cromaglutide (OBS-2020 / OBEGO™) | IND-2018-PT-0042

Dear CDER Review Division,

Panacea Therapeutics, Inc. is pleased to submit this IND Application for **cromaglutide (OBS-2020)**, a novel, long-acting GLP-1 receptor agonist for chronic management of obesity and overweight with comorbidity in adult patients.

This submission includes all components required under **21 CFR Part 312.23** and has been transmitted in **eCTD format** via the FDA Electronic Submissions Gateway (ESG), consistent with *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (Revision 8, September 2024; Table 1 mandate date for commercial INDs: **May 5, 2018**).

We respectfully request assignment to the **Division of Metabolism and Endocrinology Products (DMEP)** within CDER.

Respectfully submitted,

Aastha Dave
Lead, Regulatory Affairs
Panacea Therapeutics, Inc.

PANACEA THERAPEUTICS

3. Introductory Statement

Section Owner: Regulatory Affairs CFR Ref: 21 CFR §312.23(a)(3)

3.1 Drug Identification and Classification

Cromaglutide (OBEGO™; OBS-2020) is a novel synthetic peptide analogue of human GLP-1, classified as a **GLP-1 receptor agonist**. A proprietary C-18 fatty diacid acylation at lysine-26 confers albumin binding and $t_{\frac{1}{2}} \approx 168$ h, supporting once-weekly subcutaneous dosing.

Attribute	Details
Established Name	Cromaglutide
Proposed Trade Name	OBEGO™
Pharmacological Class	GLP-1 Receptor Agonist
Approx. Molecular Weight	∼4,113 Da
Route / Frequency	Subcutaneous; once weekly
Proposed Strengths	2.5 mg, 5 mg, 10 mg per 0.5 mL

3.2 Proposed Indication

Adjunct to reduced-calorie diet and physical activity for chronic weight management in:

- Adults with **obesity** (BMI $\geq$30 kg/m^2), OR
- Adults with **overweight** (BMI $\geq$27 kg/m^2) with $\geq$1 weight-related comorbidity (e.g., hypertension, T2DM, dyslipidaemia, OSA, CVD)

3.3 Regulatory Status

Cromaglutide is a **New Molecular Entity (NME)**. This is the first regulatory filing for OBS-2020 globally. No prior IND, NDA, or foreign marketing authorisation exists.

4. General Investigational Plan

Section Owner: Regulatory Affairs CFR Ref: 21 CFR §312.23(a)(3)(iv)

4.1 Rationale

Obesity affects ∼42% of U.S. adults. Approved GLP-1 RAs carry a class-wide boxed warning for thyroid C-cell tumour risk and are associated with substantial weight regain on cessation. Cromaglutide's preclinical profile — characterised by absence of thyroid C-cell findings and prolonged weight-loss maintenance — supports investigation as a differentiated therapeutic.

4.2 Phase 1 (Proposed: 2018–2019)

- Randomised, double-blind, placebo-controlled SAD/MAD study; $N = 80$

- Population: healthy adults and adults with obesity (BMI 27–40), ages 18–65
- Primary objectives: Safety, tolerability, PK/PD profile
- Protocol: PT-CROMA-001

4.3 Phase 3 CERES Programme (Planned: 2021–2023)

Trial	Design	N	Duration	Primary Endpoint
CERES-1	vs. Placebo, DB, R, PC	1,200	52 wks	Mean % weight change; $\geq$5% responder
CERES-2	vs. Semaglutide, DB, R	1,100	68 wks	% weight change; maintenance duration
CERES-3	LT safety extension	900	104 wks	Long-term safety; durability
CERES-CARDIO	CV outcomes	2,400	3 yrs	MACE non-inferiority

DB = double-blind; R = randomised; PC = placebo-controlled; LT = long-term.

5. Administrative Information

Section Owner: Regulatory Affairs eCTD Ref: Module 1 (FDA Backbone Spec.)

5.1 Drug Nomenclature

Nomenclature	Details
USAN / INN (proposed)	Cromaglutide
CAS Registry Number	Pending assignment
Structural Class	39-aa synthetic peptide; GLP-1 analogue with C-18 fatty diacid modification
Molecular Formula	$C_{187}H_{291}N_{45}O_{58}$ (approx.)

5.2 Table of Contents

Section	Title	Prepared By
Form FDA 1571	IND Cover Form	Regulatory Affairs
Cover Letter	Submission Intent	Regulatory Affairs
Introductory Statement	Drug Overview	Regulatory Affairs
General Investigational Plan	Rationale and Phase Plan	Regulatory Affairs
Administrative Info	Nomenclature, ToC	Regulatory Affairs
Investigator's Brochure	Preclinical Summary	*Medical Affairs*
Clinical Protocol	Phase 1 SAD/MAD Protocol	*Clinical Affairs*
CMC Information	Drug Substance & Product	RA (with CMC team)
Pharm. & Tox.	Nonclinical Summaries	*Nonclinical/Tox*
Previous Human Experience	Prior Clinical Data	*Clinical Affairs*
Form FDA 1572 / 3674	Investigator & User Fee Certs	Regulatory Affairs

5.3 Environmental Assessment — Categorical Exclusion

Per **21 CFR §25.31(e)**, Panacea Therapeutics claims a categorical exclusion. Cromaglutide is administered at 2.5–10 mg SC once weekly; estimated environmental concentration is below the threshold of regulatory concern. Full justification in *Appendix 1.2-A*.

6. Form FDA 1572 & 3674

Section Owner: Regulatory Affairs CFR Ref: 21 CFR §312.53(c); FDAAA §801

Executed FDA 1572 forms for all investigators in Protocol PT-CROMA-001 are in *Appendix 1.3*, containing investigator CVs, facility and IRB details, and all commitments per 21 CFR §312.53(c).

FDA 3674 certifies ClinicalTrials.gov compliance per 42 U.S.C. §282(j). Protocol PT-CROMA-001 will be registered prior to enrolment of the first subject.

Authorised Signatory: Aastha Dave, Lead Regulatory Affairs **Date:** March 14, 2018

7. CMC Information

Section Owner: Regulatory Affairs (with CMC/Manufacturing Team) CFR Ref: 21 CFR §312.23(a)(7); eCTD Module 3

7.1 Drug Substance

Attribute	Description
Manufacturing Site	Panacea Therapeutics API Facility, Cambridge, MA (FDA-registered)
Synthesis	Fmoc SPPS with solution-phase acylation
Purity Specification	$\geq$98.0% by RP-HPLC
Impurities	Any individual $\leq$0.5%; total $\leq$1.5%
Storage	$-20\,^{\circ}$C $\pm$ 5 °C, protected from light

7.2 Drug Product

Attribute	Description
Dosage Form	Sterile solution for SC injection
Container Closure	Single-dose, Type I glass pre-filled syringe with needle safety device
Strengths	2.5 mg, 5 mg, 10 mg per 0.5 mL
Excipients	Sodium phosphate buffer, NaCl, polysorbate 80, phenol, WFI
Proposed Shelf Life	24 months at 2–8 °C; 28 days at $\leq$30 °C in-use

7.3 Analytical Controls

Test	Method	Specification
Identity	Peptide mapping / MS	Conforms
Assay	RP-HPLC	97.0–103.0%
Purity	RP-HPLC	Total $\leq$1.5%
Bioactivity	GLP-1R cell-based assay	80–125% of reference
Sterility	USP <71>	No growth
Endotoxin	LAL / USP <85>	$<$1.0 EU/mL
Particulates	USP <788>	Meets compendial limits

8. Investigator's Brochure

Section Owner: Medical Affairs

Complete IB (v1.0, February 2018) compiled per ICH E6(R2) to be provided by Medical Affairs. *Summary:* Preclinical pharmacology, GLP-compliant toxicology (4-week rat, 13-week NHP), safety pharmacology, and PK characterisation. Key finding: no thyroid C-cell hyperplasia or MTC observed, supporting absence of a boxed warning.

9. Clinical Protocol PT-CROMA-001

Section Owner: Clinical Affairs / Biostatistics

Full protocol (v1.0, February 28, 2018) to be provided by Clinical Affairs. *Summary:* Phase 1 SAD/MAD; $N \leq 80$; BMI 27–40; ages 18–65. Seven cohorts (SAD: 0.5–5 mg; MAD: 2.5–10 mg QW). Primary endpoints: safety, tolerability, PK/PD. AEs graded per CTCAE v5.0; DSMB established.

10. Pharmacology and Toxicology

Section Owner: Nonclinical/Toxicology

Complete GLP-compliant study reports (21 CFR Part 58) to be provided by Nonclinical team. *Summary:* GLP-1R agonism confirmed (EC_{50} = 0.03 nM); safety pharmacology

core battery negative; NOAEL established in rat and NHP; no genotoxicity; no thyroid C-cell findings.

11. Previous Human Experience

Section Owner: Clinical Affairs

First-in-human application; cromaglutide has not previously been administered to humans. Clinical Affairs will provide class-level GLP-1 RA human data to contextualise the safety monitoring plan for Protocol PT-CROMA-001.