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PANACEA THERAPEUTICS, INC.

A biopharma company dedicated to a healthy world.

NEW DRUG APPLICATION (NDA)

505(b)(1) Full Application | ICH M4 CTD | eCTD Rev. 8 (Sep 2024)

Cromaglutide (OBEGO™)

Internal Code: OBS-2020

Field	Details
NDA Number	NDA 218-947
Submission Date	October 3, 2023
Application Type	505(b)(1) — NME
Regulatory Lead	Aastha Dave, Lead RA
Priority Designation	Fast Track; BTD
Proposed PDUFA Date	October 3, 2024
eCTD Standard	ICH v3.2.2 / v4.0 (FDA Rev. 8, Sep 2024)

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Fictional portfolio sample for educational purposes only. Not an actual FDA submission.

Portfolio Note: Sections labelled **[RA-Authored]** reflect Regulatory Affairs content. Sections labelled **[Other Function]** are summarised at high level only. Submitted in **eCTD format** via the FDA ESG per FDA guidance *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, eCTD for NDAs became mandatory **May 5, 2017**. Datasets placed in Modules 3, 4, and 5 only (Sec. III.L of Revision 8).

Contents

Module 1: Administrative Information & Prescribing Information

Section Owner: Regulatory Affairs CFR Ref: 21 CFR §314; eCTD Module 1

1.1 Form FDA 356h

Field	Details
Sponsor	Panacea Therapeutics, Inc.
Application Type	NDA — 505(b)(1)
Proposed Trade Name	OBEGO™
Established Name	Cromaglutide
Dosage Form / Route	Solution for subcutaneous injection
Strengths	2.5 mg, 5 mg, 10 mg per 0.5 mL
Proposed Indication	Adjunct to reduced-calorie diet and physical activity for chronic weight management in adults with obesity (BMI $\geq$30) or overweight (BMI $\geq$27) with $\geq$1 comorbidity
Reference Listed Drug	N/A — New Molecular Entity
Priority Designation	Fast Track (June 2019); BTD (March 2021)
NCE Exclusivity	Requested — 21 USC §355(c)(3)(E)(ii)
Authorized Signatory	Aastha Dave, Lead Regulatory Affairs
Submission Date	October 3, 2023

1.2 Cover Letter

Date: October 3, 2023
To: DMEP, CDER, U.S. FDA
From: Aastha Dave, Lead Regulatory Affairs, Panacea Therapeutics, Inc.
Re: NDA Submission — Cromaglutide (OBEGO™) | NDA 218-947

Panacea Therapeutics, Inc. is pleased to submit this 505(b)(1) NDA for **cromaglutide (OBEGO™)**, supported by 8 completed clinical studies including two pivotal

Phase 3 trials. The submission has been prepared in **eCTD format** and transmitted via the FDA 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; mandatory for NDAs since **May 5, 2017**).

Key milestones: Pre-IND Nov 2017 → IND Apr 2018 → Fast Track Jun 2019 → EOP2 Dec 2020 → BTD Mar 2021 → Pre-NDA Jan 2023 → **NDA Oct 2023 (eCTD Seq. 0000)** → PDUFA Oct 2024.

Standard Review is respectfully requested. All user fees paid (Form FDA 3397 enclosed). No eCTD waiver required.

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1.3 Comprehensive Table of Contents

Mod.	Sec.	Title	Owner
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1	1.2	Cover Letter	Regulatory Affairs
1	1.3	Table of Contents	Regulatory Affairs
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1	1.5	Patent & Exclusivity Certifications	Regulatory Affairs
1	1.6–1.8	Debarment, Field Copy, User Fee Certs	Regulatory Affairs
1	1.9	Financial Disclosure (FDA 3455)	RA (compiled)
1	1.10	Environmental Assessment / Cat. Excl.	Regulatory Affairs
1	1.11	Paediatric Study Plan (iPSP)	Regulatory Affairs
2	2.3	Introduction to Summary Documents	Regulatory Affairs
2	2.4	Nonclinical Overview	*Nonclinical/Tox*
2	2.5	Clinical Overview	RA (with Clinical input)
2	2.6	Nonclinical Summaries	*Nonclinical/Tox*
2	2.7	Clinical Summary	RA (with Clinical input)
3	3.2	Body of Data — CMC	RA (with CMC team)
4	4.2	Nonclinical Study Reports	*Nonclinical/Tox*
5	5.3	Clinical Study Reports	*Clinical / Biostatistics*

1.4 Proposed Labeling — Draft Package Insert (PLR Format)

Prepared per 21 CFR Part 201 and PLR format (21 CFR §§201.56–201.57). Final labeling subject to FDA negotiation.

HIGHLIGHTS OF PRESCRIBING INFORMATION

See full prescribing information for OBEGO™.

OBEGO™ (cromaglutide) injection, for subcutaneous use
Initial U.S. Approval: 2024 (anticipated)

INDICATIONS AND USAGE (1)

OBEGO™ is a GLP-1 receptor agonist indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with:

- BMI $\geq$30 kg/m^2 (obesity), or
- BMI $\geq$27 kg/m^2 (overweight) with $\geq$1 weight-related comorbidity (hypertension, T2DM, dyslipidaemia, OSA)

DOSAGE AND ADMINISTRATION (2)

- Start: 2.5 mg SC once weekly $\times$ 4 weeks; escalate to 5 mg then 10 mg as tolerated
- Rotate injection sites (abdomen, thigh, upper arm)

CONTRAINDICATIONS (4): Personal/family history of MTC; MEN-2; hypersensitivity.

WARNINGS AND PRECAUTIONS (5): Pancreatitis (5.1); diabetic retinopathy (5.2); heart rate increase (5.3); hypoglycaemia with secretagogues (5.4); GI adverse reactions (5.5); suicidal ideation (5.6).

ADVERSE REACTIONS (6): Most common ($\geq$5%): nausea, diarrhoea, vomiting, constipation, abdominal pain, fatigue, injection site reactions.

Labeling Differentiation Note (RA Strategy): Unlike semaglutide (WEGOVY®) and liraglutide (SAXENDA®), **OBEGO™ carries no Boxed Warning for thyroid C-cell tumour risk.** Cromaglutide showed no thyroid C-cell hyperplasia or MTC in 2-year rat or 6-month transgenic mouse carcinogenicity studies — a significant labeling and promotional advantage central to Panacea's regulatory strategy.

1.5 Patent and Exclusivity Certifications

Type	Detail	Expiry
Composition of matter	US 10,XXX,XXX — Cromaglutide structure and acylation	2038
Method of use	US 10,XXX,XXX — Use for weight management	2040
NCE Exclusivity	5-year per 21 USC §355(c)(3)(E)(ii)	2029

1.6 Environmental Assessment — Categorical Exclusion

Per **21 CFR §25.31(e)**, categorical exclusion claimed. Cromaglutide at 2.5–10 mg SC weekly; estimated environmental concentration below threshold of concern. Full justification: *Appendix 1.10-A*.

1.7 Paediatric Study Plan (iPSP)

Agreed iPSP accepted February 2022 per PREA / 21 CFR §314.55.

- **Deferral:** Adolescent trial (CERES-PEDS, ages 12–17) to begin post-approval Q1 2025
- **Waiver:** Ages <12 waived; obesity pharmacotherapy not appropriate in this age group

Module 2: Summaries

Section Owner: RA (2.3, 2.5, 2.7); Nonclinical/Tox (2.4, 2.6) eCTD Module 2

2.1 2.3 Introduction [RA-Authored]

This 505(b)(1) NDA relies entirely on studies conducted by or for Panacea Therapeutics. Prepared in **ICH M4 CTD format** as **eCTD** per Revision 8 (September 2024). Datasets placed in Modules 3, 4, and 5 only per Section III.L. All four regulatory questions from the End-of-Phase 2 meeting (December 2020) have been met.

2.2 2.4 Nonclinical Overview

Section Owner: Nonclinical/Toxicology. Complete overview per ICH M4S. *Summary:* Potent GLP-1R agonism (EC_{50} = 0.03 nM); DIO murine efficacy

(up to 22% body weight reduction); clean safety pharmacology. **No thyroid C-cell hyperplasia or MTC** in 2-year rat or 6-month transgenic mouse studies — supports absence of boxed warning.

2.3 2.5 Clinical Overview [RA-Authored — with Clinical input]

2.3.1 Clinical Development Summary

Study	Ph.	N	Duration	Key Outcome
PT-CROMA-001	1	80	12 wks	Safe/tolerable; $t_{\frac{1}{2}} \approx 168$ h
PT-CROMA-101	2	318	28 wks	10 mg QW selected; -13.4% weight loss
CERES-1	3	1,210	52 wks	-16.8% vs. -2.4% ($p < 0.0001$)
CERES-2	3	1,106	68 wks	Superiority vs. semaglutide; lower rebound
CERES-3	3	892	104 wks	1 serious TEAE; sustained efficacy; no MTC
CERES-CARDIO	3	2,418	3 yrs	Non-inferior MACE; ongoing

Total exposure: 6,088 subjects; $\sim$9,842 patient-years

2.3.2 Benefit–Risk Assessment

Benefits	
Efficacy vs. Placebo	−16.8% mean weight change; 86.3% ≥5% weight loss (p <0.0001)
vs. Semaglutide	−17.3% vs. −14.9% at Wk 68 (p = 0.0014)
Maintenance	54.2 weeks vs. 41.6 weeks (p <0.001)
Rebound	28.4% vs. 56.2% weight regained post-cessation (p <0.001)
Labeling	**No boxed warning** — key differentiator from GLP-1 RA class
Risks	
GI AEs	44.2%; mostly mild–moderate, transient during dose escalation
Pancreatitis	0.3%; consistent with GLP-1 RA class
Discontinuation	9.3% due to AEs
Hypoglycaemia	5.8% in T2DM patients on secretagogues

2.4 2.6 Nonclinical Written & Tabulated Summaries

Section Owner: Nonclinical/Toxicology. Per ICH M4S.

2.5 2.7 Clinical Summary [RA-Authored — with Clinical input]

2.5.1 CERES-1 — Pivotal Efficacy vs. Placebo (Week 52)

Endpoint	OBEGO 10 mg	Placebo	p-value
Mean % weight change	−16.8%	−2.4%	<0.0001
≥5% weight loss	86.3%	32.1%	<0.0001
≥10% weight loss	71.4%	14.8%	<0.0001
≥15% weight loss	48.2%	5.3%	<0.0001
Mean absolute weight loss	−18.3 kg	−2.6 kg	<0.0001

2.5.2 CERES-2 — vs. Semaglutide 2.4 mg (Week 68)

Endpoint	OBEGO 10 mg	Sema 2.4 mg	p-value
Mean % weight change (Wk 68)	−17.3%	−14.9%	0.0014
Maintenance duration	54.2 wks	41.6 wks	$<$0.001
Rebound weight gain	28.4%	56.2%	$<$0.001

2.5.3 Integrated Safety (N = 6,088)

Safety Parameter	OBEGO (any dose)	Placebo/Comparat
Any AE	78.4%	62.1%
GI AEs	44.2%	18.7%
Serious AEs	8.1%	6.9%
Discontinuation	9.3%	4.2%
Pancreatitis	0.3%	0.1%
Hypoglycaemia (T2DM)	5.8%	2.2%
Thyroid C-cell tumours/MTC	**0**	0
MACE	Non-inferior	Reference

Module 3: Quality / CMC

> **Section Owner: Regulatory Affairs (with CMC/Manufacturing Team)** eCTD Module 3; datasets in Module 3 only (Sec. III.L)

3.1 3.2.S — Drug Substance

Attribute	Detail
Manufacturing Site	Panacea API Facility, Cambridge, MA (FDA-registered; EMA-inspected)
Synthesis	Fmoc SPPS; solution-phase acylation; prep. RP-HPLC
Batch Size	5 kg
Process Validation	3 PPQ batches (PT-API-VAL-2023-001)

Control of Drug Substance:

Test	Method	Specification
Identity	Peptide mapping / LC-MS	Conforms
Assay	RP-HPLC (PT-DS-002)	97.0–103.0%
Purity	RP-HPLC (PT-DS-003)	Total $\leq$1.5%
Bioactivity	GLP-1R cell-based (PT-DS-005)	80–125% of reference
Elemental impurities	ICP-MS (PT-DS-006)	Meets ICH Q3D

3.2 3.2.P — Drug Product

Description: Sterile, clear, colorless to slightly yellow aqueous SC injection solution in single-dose Type I glass pre-filled syringes with staked needle and passive safety device.

Control of Drug Product:

Test	Method	Specification
Assay	RP-HPLC (PT-DP-002)	95.0–105.0% of label claim
Degradation products	RP-HPLC (PT-DP-003)	Specified ≤1.0%
pH	USP <791>	7.0–8.0
Particulate matter	USP <788>	Meets compendial limits
Sterility	USP <71>	No growth
Endotoxins	LAL USP <85>	<1.0 EU/mL

Stability:

Condition	Data Duration	Conclusion
Long-term: 2–8 ℃/ambient RH	36 months	Supports 24-month shelf life
Accelerated: 25 ℃ / 60% RH	12 months	No significant degradation
In-use: ≤30 ℃	28 days	Supports in-use labeling

Module 4: Nonclinical Study Reports

Section Owner: Nonclinical/Toxicology. Complete GLP-compliant study reports per ICH M4S (21 CFR Part 58). Studies include: GLP-1R pharmacology; DIO murine efficacy; safety pharmacology (ICH S7A/S7B); 26-week rat and 52-week NHP toxicology; 2-year rat and 6-month transgenic mouse carcinogenicity; reproductive toxicology (Segments I–III); genotoxicity panel. All nonclinical datasets in Module 4 only per eCTD Revision 8 Sec. III.L.

Module 5: Clinical Study Reports

Section Owner: Clinical Affairs / Biostatistics. Complete CSRs for all 8 studies per ICH M4E / ICH E3. Pivotal: CERES-1 (52 weeks vs. placebo), CERES-2 (68 weeks vs. semaglutide), CERES-3 (104-week extension). SAPs, randomisation codes, and data listings included as CSR appendices. All clinical datasets in Module 5 only per eCTD Revision 8 Sec. III.L. RA contributed regulatory input on CSR structure, labeling-relevant endpoint selection, and integrated safety narrative.

NDA Submission Date: *October 3, 2023* ***Regulatory Lead:*** *Aastha Dave* ***PANACEA THERAPEUTICS, INC.***