RBP-6000 Buprenorphine Monthly Depot Demonstrates Efficacy, Safety, and Exposure-Response Relationship in Adults with Opioid Use Disorder: Results from a Phase III Clinical Trial

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RBP-6000 is an investigational new drug, not currently authorized for marketing for any indication.

Disclosure/Conflict of Interest

All authors are employees of Indivior Inc., which sponsored this study.

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RBP-6000: Long-Acting Subcutaneous Injection Administered Monthly by HCP in Health Care Setting

ATRIGEL® Delivery System

- Biodegradable polymer and solvent create solid depot of buprenorphine
- Two targeted release phases: rapid achievement of therapeutic levels that are sustained over monthly dosing interval
- Used in 7 FDA-approved products
- Prefilled syringe, administered subcutaneously

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Development Objectives for RBP-6000

- **Achieve opioid blockade**
  - from the first dose and across the entire monthly dosing interval
  - at buprenorphine plasma concentrations that are well-tolerated
- **Achieve clinically significant control of craving and withdrawal symptoms**
- **Prevent illicit opioid use**
- **Limit possibility of abuse/misuse, diversion, and accidental overdose**

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Overview of RBP-6000 Clinical Development Program

- **Utilized science on relationship between buprenorphine plasma levels, mu-opioid receptor occupancy (μORO), and clinical effects to maximize benefits for patients with OUD**

First-in-Human (FIH) Study
(20 mg)

Single Ascending Dose (SAD) Study
(50, 100, 200 mg)

Multiple Ascending Dose (MAD) Study
(50, 100, 200, 300 mg)

Molecular Weight (MW) Study
(300 mg)

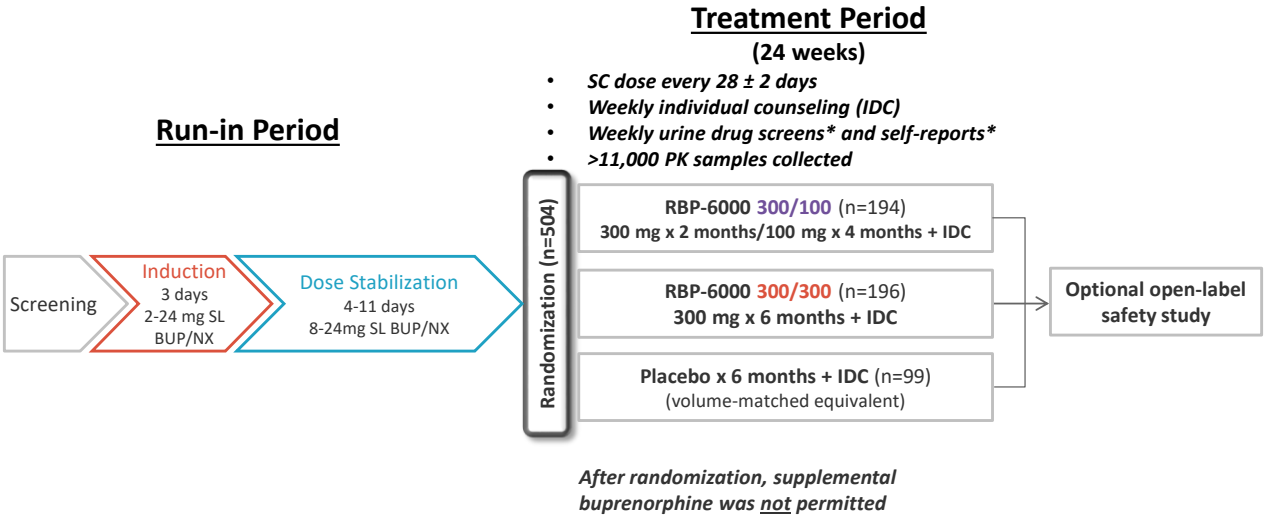
Opioid Blockade (OB) Study
(300 mg)

Phase 3 Double-Blind Placebo-Controlled Study
(300/100, 300/300 mg)

Phase 3 Long-Term Open-Label Safety Study
(300 mg → Flex dosing)

Treatment Extension Study
(Flex dosing)

Phase 3 Study (RB-US-13-0001) Design



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**Missing data treated as "non-negative"*

Key Inclusionary / Exclusionary Criteria

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- Meet DSM-5 criteria for moderate or severe OUD
- Seeking medication-assisted treatment (MAT)
- No MAT for OUD within 90 days
- Age 18-65 years
- BMI 18-35 kg/m^2

Key Exclusionary Criteria

- Current diagnosis other than OUD requiring chronic opioid treatment
- Use of buprenorphine, methadone, or benzodiazepines 30 days before screening
- Recent history of suicidality
- Significant medical problems

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Demographic Characteristics

	RBP-6000 300/300 mg + IDC N=196	RBP-6000 300/100 mg + IDC N=194	Placebo + IDC N=99
Age, years (mean, range)	39 (19-64)	40 (20-64)	39 (20-63)
Male, %	67	66	65
Race, %			
White	71	68	78
Black or African American	28	29	20
American Indian or Alaska Native	<1	2	1
Multiple	<1	1	1
Hispanic or Latino Ethnicity, %	9	6	10

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History of Opioid Use at Baseline

	RBP-6000 300/300 mg + IDC N=196	RBP-6000 300/100 mg + IDC N=194	Placebo + IDC N=99
Severity of OUD, %			
Moderate	34	25	31
Severe	65	73	68
Duration of Opioid Use, years			
Mean (SD)	11 (9)	12 (10)	11 (9)
Users by Route, %			
Injecting Users	41	43	51
Non-injecting Users	59	57	49

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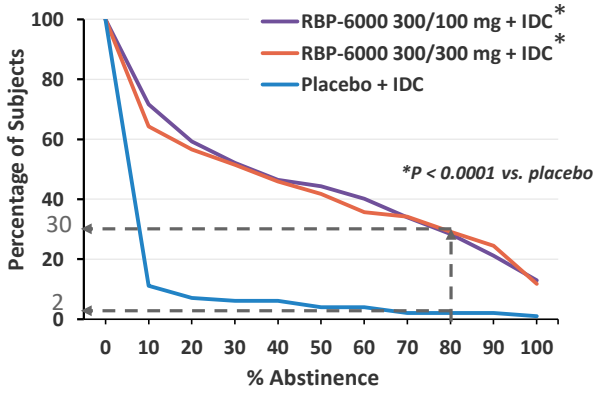
Primary Efficacy Endpoint (Cumulative Distribution Function of Percentage Abstinence)

Primary endpoint (% Abstinence): % urine samples negative for opioids + negative self-reports of illicit opioid use (Weeks 5 to 24)



Mean Percentage Abstinence	
RBP-6000 300/100 mg + IDC (n=194)	42.7%
RBP-6000 300/300 mg + IDC (n=196)	41.3%
Placebo + IDC (n=99)	5.0%

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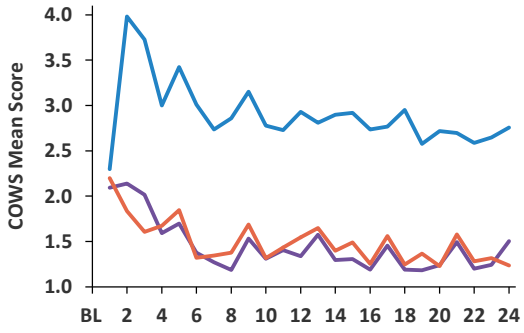
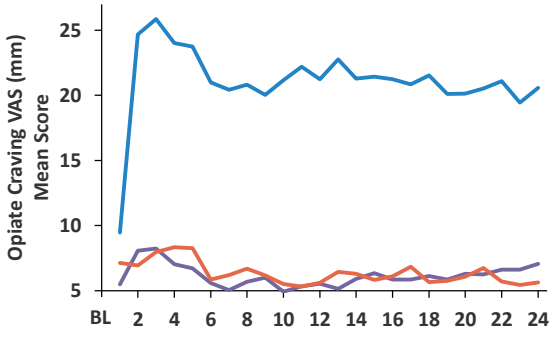
Secondary Endpoints

Clinical Opiate Withdrawal Scale (COWS)



Opioid Craving Visual Analog Scale (VAS)



RBP-6000 300/300 mg + IDC (n=196)
RBP-6000 300/100 mg + IDC (n=194)
Placebo + IDC (n=99)

BL, baseline.

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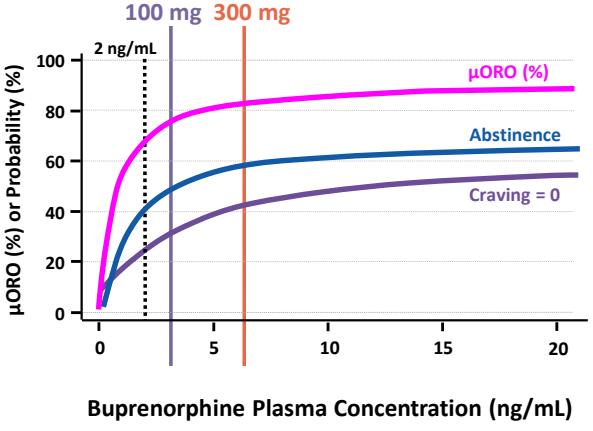
Summary of Relationship Between Plasma Buprenorphine Concentrations and Clinical Endpoints



Dose Group	N	C_{avg} (ng/mL)	μORO (%)*
RBP-6000 300/100 mg + IDC	194	3.14	75
RBP- 6000 300/300 mg + IDC	196	6.32	83

* Predicted whole brain μ-Opioid Receptor Occupancy corresponding to C_{avg}

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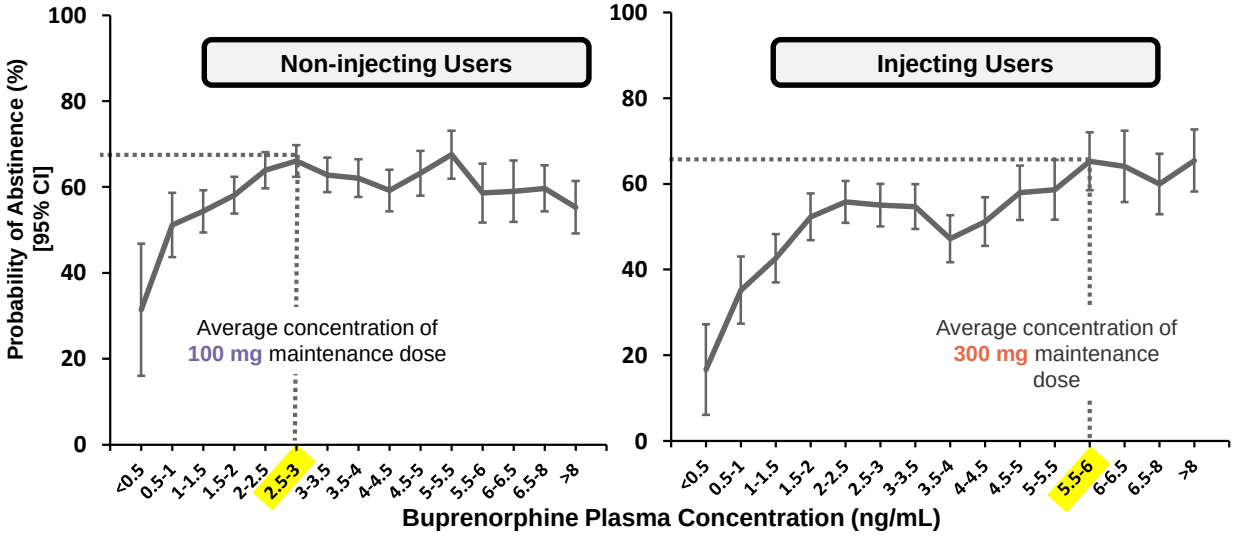
Exposure-response Analysis by Injecting Status



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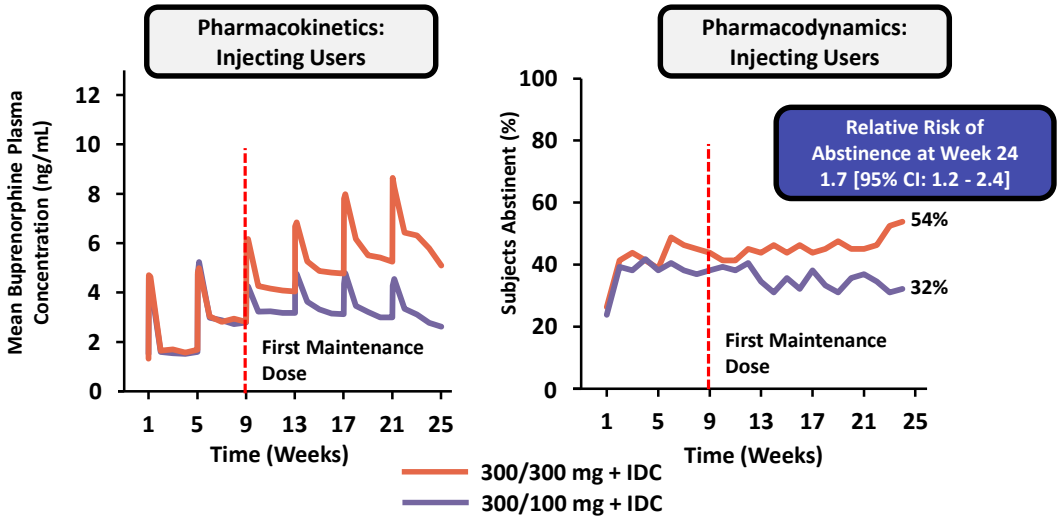
11,362 PK Samples from Phase 3 Double-blind Study

PK and PD Relationship for The Two Maintenance Doses Among Injecting Opioid Users



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Safety Results

- No new or unexpected safety findings; generally well-tolerated
- No serious injection site reactions
- 1 subject discontinued treatment due to injection site reaction

Occurrence (%)	RBP-6000 300/300 mg + IDC (N=201)	RBP-6000 300/100 mg + IDC (N=203)	Placebo + IDC (N=100)
Any TEAE	66.7	76.4	56.0
Serious TEAE	3.5	2.0	5.0
TEAE leading to discontinuation	5.0	3.4	2.0
Any injection site TEAE	18.9	13.8	9.0
Serious injection site TEAE	0	0	0
Injection site TEAE leading to discontinuation	0.5	0	0

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Use of Other Substances did not Increase During Phase 3 Double-Blind Study

	RBP-6000 300/300 mg + IDC N=194		RBP-6000 300/100 mg + IDC N=196		Placebo + IDC N=99	
Substance, %	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Amphetamines	15	7 – 12	25	11 – 22	19	5 – 19
Barbiturates	1	0 – 2	2	0 – 2	0	0 – 3
Benzodiazepines	10	3 – 9	12	3 – 10	13	3 – 20
Cocaine	40	27 – 39	47	25 – 33	42	20 – 45
Cannabinoids	47	28 – 38	55	28 – 39	53	32 – 43
Phencyclidine	1	1 – 4	0	0 – 2	1	0 – 6

Follow-up use is shown as the range of observed values over follow-up.
Use defined as positive UDS, positive self-report on TLFB, or concomitant medication.
TLFB, timeline followback; UDS, urine drug screen.

Use decreased
No change
Use increased

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Summary

- Both dosage regimens of RBP-6000 showed statistically significant differences in percentage abstinence and treatment success versus placebo
- Treatment outcomes were consistent across other clinical endpoints including control of craving and withdrawal symptoms
- Results from the exposure-response analyses predicted a relationship between buprenorphine plasma concentrations, predicted whole brain mu-opioid receptor occupancy, abstinence, and opioid craving
- Subgroup findings consistent with prior scientific literature that some subjects may benefit from higher buprenorphine exposure to maximize abstinence
- The safety profile of RBP-6000 was consistent with the known profile of transmucosal buprenorphine, with no unexpected safety findings; injection site reactions were not treatment-limiting and the use of other substances did not increase

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Acknowledgements

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