

## Connecting Innovation to Purpose

**Corporate Presentation** March 28, 2024



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#### **Investment Summary**



## Focus on developing precision oncology + differentiated assets



Nectin-4 targeting ADC for treatment of solid tumors



CB1R inverse agonist to treat obesity



TGF $\beta$  blocker Anti- $\alpha$ v $\beta$ 8 integrin mAb for treatment of solid tumors

## **CRBP**Ticker

#### \$127 Million

Cash & investments as of Feb 2, 2024 10.3M Common Shares Outstanding (11.1M Fully-Diluted Shares)

#### A diversified pipeline with differentiated clinical risk profiles



Next-Generation Nectin-4 targeting ADC					
CRB-701 Nectin-4 po	Nectin-4 positive	<b>CSPC</b> (China)	Dose Escalation Cohorts 1-6 completed Cohort 7 added and recruiting	<b>Dose Confirmation / Expansion</b> Cohort 6 expanding	
Next-generation Nectin-4 targeting ADC	solid tumors	Corbus (US + Europe)  Dose Escalation		Dose Confirmation / Expansion	
Anti-Integrin mAb					
CRB-601 Anti-ανβ8 mAb (TGF6-targeting) ανβ8 enriched solid tumors		IND Cleared in	January 2024		
Highly peripherally-restricted CB1R inverse agonist					
CRB-913 CB1R inverse agonist	Ubesity and related conditions		IND Expected in Q4 2024		

# CRB-701 Next Generation Nectin-4 Targeting ADC

#### Padcev<sup>®</sup> projected to reach up to ~\$5B in global sales by 2028





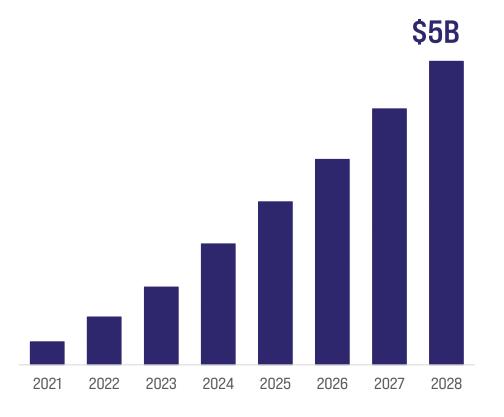
#### Latest Padcev® Q3 revenues 1

	Three	months er	ided Sept	ember 30,	Nine m	nonths ende	d Septer	nber 30
(dollars in millions)	2023	2022	% Char	nge	2023	2022	% Cha	nge
<b>Total Net Product Sales</b>	\$ 571	\$ 428	33	%	\$ 1,583	\$ 1,243	27	%
ADCETRIS	\$ 246	\$ 219	13	%	\$ 751	\$ 601	25	%
PADCEV	\$ 200	\$ 105	89	%	\$ 479	\$ 329	46	%
TUKYSA	\$ 102	\$ 88	16	%	\$ 289	\$ 267	8	%
TIVDAK	\$ 23	\$ 16	40	%	\$ 64	\$ 45	42	%

#### 22<sup>nd</sup> October 2023<sup>2</sup>

Groundbreaking EV-302 Trial Significantly Extends Overall Survival and Progression-Free Survival in Patients Treated with PADCEV® (enfortumab vedotin-ejfv) and KEYTRUDA® (pembrolizumab) in First-Line Advanced Bladder Cancer

### PADCEV® Global Projected Revenues in UC/Bladder³



#### Does tolerability for Padcev® impact clinical adoption?



#### **PADCEV®** Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use

Initial U.S. Approval: 2019

#### WARNING: SERIOUS SKIN REACTIONS See full prescribing information for complete boxed warning.

- PADCEV can cause severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Immediately withhold PADCEV and consider referral for
- specialized care for suspected SJS or TEN or severe skin reactions. Permanently discontinue PADCEV in natients with confirmed
- SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions. (2.2), (5.1) (6.1)

- RECENT MAJOR CHANGES -Indications and Usage (1)

- INDICATIONS AND USAGE -PADCEV is a Nectin-4-directed antibody and microtubule inhibitor conjugate

- . as a single agent for the treatment of adult patients with locally advanced or metastatic urothelial cancer who: ously received a programmed death receptor-1 (PD-1) or
- aining chemotherapy, or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy. (1) in combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer who are not
- eligible for cisplatin-containing chemotherapy. (1) response rate and durability of response. Continued approval for this
- indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. (14.1) --- DOSAGE AND ADMINISTRATION ---
- · For intravenous infusion only. Do not administer PADCEV as an ntravenous push or bolus. Do not mix with, or administer as an infusion with, other medicinal products. (2.3)
- The recommended dose of PADCEV as a single agent is 1.25 mg/kg (up to a maximum dose of 125 mg) given as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity. (2.1)
- The recommended dose of PADCEV in combination with pembrolizumab is 1.25 mg/kg (up to a maximum dose of 125 mg) given as an intravenous infusion over 30 minutes on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity. (2.1)
- Avoid use in patients with moderate or severe hepatic impairment (8.6) - DOSAGE FORMS AND STRENGTHS -For Injection: 20 mg and 30 mg of enfortumab vedotin-ejfv as a lyophilized

powder in a single-dose vial for reconstitution. (3)

CONTRAINDICATIONS

- WARNINGS AND PRECAUTIONS Hyperelycemia: Diabetic ketoacidosis may occur in patients with and
- without preexisting diabetes mellitus, which may be fatal. Closely monitor blood glucose levels in patients with, or at risk for, diabete mellitus or hyperglycemia. Withhold PADCEV if blood glucose is
- >250 mg/dL. (2.2, 5.2)
  Pneumonitis/Interstitial Lung Disease (ILD): Severe, life-threatening fatal pneumonitis/ILD may occur. Withhold PADCEV for Grade 2 oneumonitis/ILD and consider dose reduction. Permanently discontinu PADCEV for Grade 3 or 4 pneumonitis/ILD. (2.2, 5.3)

  Peripheral Neuropathy: Monitor patients for new or worse
- peripheral neuropathy and consider dose interruption, dose reduction discontinuation of PADCEV. (2.2, 5.4)

  Ocular Disorders: Ocular disorders, including vision changes, may
- occur. Monitor patients for signs or symptoms of ocular disorders. Consider prophylactic artificial tears for dry eyes and treatment with ophthalmic topical steroids after an ophthalmic exam. Consider dose interruption or dose reduction of PADCEV when symptomatic ocular
- Infusion Site Extravasation: Ensure adequate venous access prior to administration. Monitor the infusion site during PADCEV administration and stop the infusion immediately for suspected
- extravasation. (5.6) Embryo-Fetal Toxicity: PADCEV can cause fetal harm. Advise of the potential risk to a fetus and to use effective contraception. (5.7, 8.1, 8.3)

- ADVERSE REACTIONS -

- PADCEV as a single agent: rash, aspartate aminotransferase increased glucose increased, creatinine increased, fatigue, peripheral neuropathy lymphocytes decreased, alopecia, decreased appetite, hemoglobin decreased, diarrhea, sodium decreased, nausea, pruritus, phosphate decreased, dysgeusia, alanine aminotransferase increased, anemia, albumin decreased, neutrophils decreased, urate increased, lipase increased, platelets decreased, weight decreased and dry skin. (6.1)
- PADCEV in combination with nembrolizumab: glucose increases aspartate aminotransferase increased, rash, hemoglobin decreased, creatinine increased, peripheral neuropathy, lymphocytes decreased, fatigue, alanine aminotransferase increased, sodium decreased, lipase increased, albumin decreased, alonecia, phosphate decreased, decreased weight, diarrhea, pruritus, decreased appetite, nausea, dysgeusia, potassium decreased, neutrophils decreased, urinary tract infectis constipation, potassium increased, calcium increased, peripheral edema,

dry eye, dizziness, arthralgia, and dry skin. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Astellas Pharma US, Inc. at 1-800-727-7003 or FDA at 1-800-FDA-1088 or

- DRUG INTERACTIONS Concomitant use of dual P-gp and strong CYP3.44 inhibitors with PADCEV may increase the exposure to monomethyl auristatin E (MMAE). (7.1)

--- USE IN SPECIFIC POPULATIONS

See 17 for PATIENT COUNSELING INFORMATION and FDA-

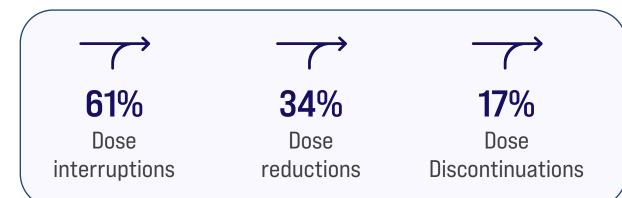
Revised: 4/2023



#### **Duration of Response** ~5 months

**47**%

Rate of Serious Adverse Events (SAEs)



#### Padcev® is associated with skin toxicities and peripheral neuropathy





#### A Black Box warning 1

#### WARNING: SERIOUS SKIN REACTIONS

- PADCEV can cause severe and fatal cutaneous adverse reactions including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which occurred predominantly during the first cycle of treatment, but may occur later.
- Closely monitor patients for skin reactions.
- Immediately withhold PADCEV and consider referral for specialized care for suspected SJS or TEN or severe skin reactions.
- Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions [see Dosage and Administration (2.2), Warnings and Precautions (5.1) and Adverse Reactions (6.1)].
- Greater than 25% of PADCEV® discontinuations are linked to peripheral neuropathy <sup>2</sup>
- PADCEV® + Keytruda® patients who experienced neuropathy:
  - 13% complete resolution
  - 87% patients had residual neuropathy (45% had Grade ≥2)¹

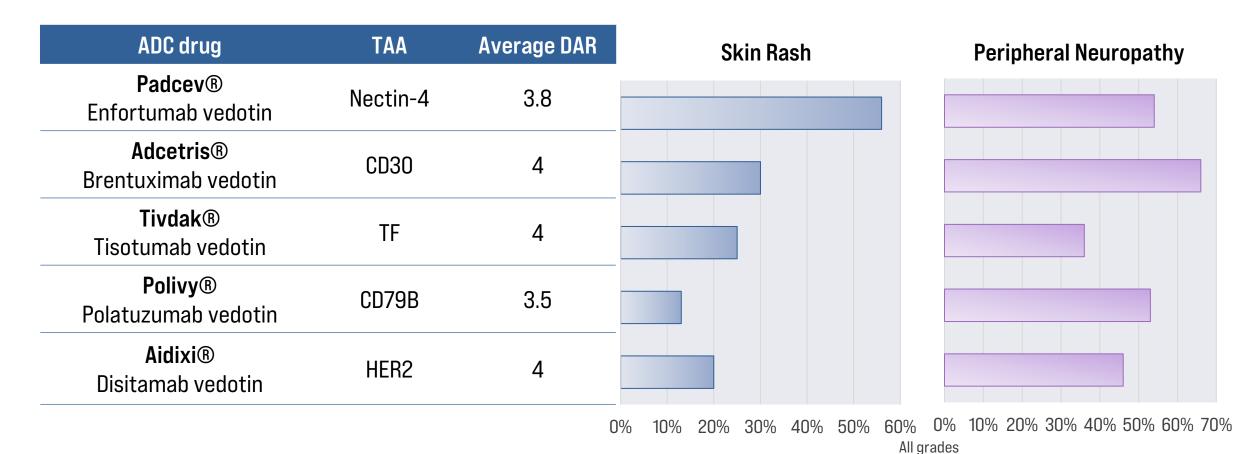
#### **Adverse Events (% of patients)**

	PADCEV® monotherapy <sup>1</sup>		PADCEV® + Keytruda®1	
	All Grades	≥ Gr 3	All Grades	≥ Gr 3
Skin Reactions	58%	14%	70%	17%
Peripheral Neuropathy	53%	5%	67%	7%

#### Is the 2<sup>nd</sup> generation Seagen linker the cause?



## Similar dose limiting toxicities seen across divergent ADCs that share same constellation of 'linker + payload' Val-Cit linker + vedotin (MMAE) payload

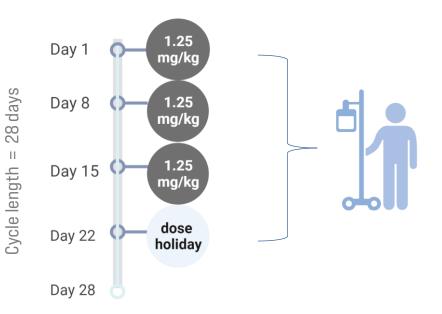




#### Padcev® requires frequent dosing and real-world usage differs from label



#### **Monotherapy Padcev®**



6 months of therapy = ~ 54 hours of total clinic time / patient

## Real-world use, dose intensity, and adherence to Padcev®

Metric	Result (N = 416)
EV use	
Number of cycles (median, IQR)	5 (2,8)
EV dose intensity	
Treatments per patient month (mean [SD])	2.6 [0.6]
Dosing frequency; treatments per cycle (mean [SD])	2.4 [0.5]
Dose (mean, mg/kg [SD])	1.1 [0.2]
Change in average dose (mg) from baseline (%)	-9.6 [20.2] %
EV treatment adherence	
Received on average > 2 treatments per cycle (%)	58.8 [34.4] %

#### Emerging clinical-stage competition is not solving for existing challenges









Limitation	<b>Padcev</b> ®	BT8009	9MW-2821
Upper dose limit	1.25 mg/kg <sup>1</sup>	5 mg/m <sup>2</sup> <sup>4</sup>	1.25 mg/kg <sup>3</sup>
Schedule	D1, D8, D15 /28 days	Q1W	D1, D8, D15 /28 days
≥ Grade 3 AE rate	51% (n=155) <sup>2</sup>	65% (n=20) <sup>6</sup>	35% (n=85) <sup>3</sup>
Peripheral neuropathy	38%	30%	17%
Skin reactions	25%	10%	18%
Neutropenia (Gr 3)	<b>5</b> % <sup>3</sup>	10%#	<b>19</b> %
Dose reduction	34%	16%	3.5%
Dose interruptions	64%	24%	28%

#### Designing a Nectin-4 ADC intended to address Padcev® unmet needs





**Toxicity**: 3<sup>rd</sup> gen ADC w/stable linker → Reduce free circulating MMAE



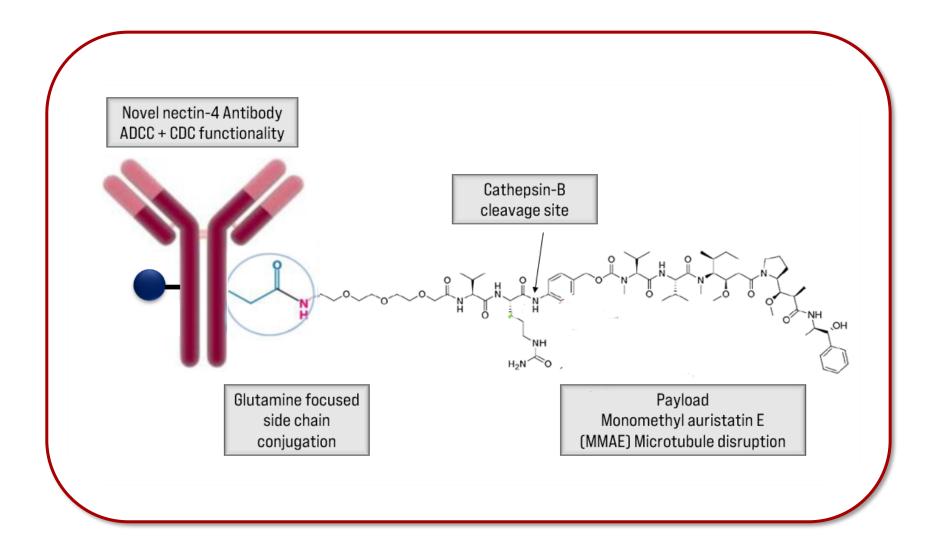
**Compliance**: Extend ADC half-life → Reduce dosing frequency



**Efficacy**: Lower DAR + longer half-life → Dose higher than Padcev®

#### **CRB-701:** Next generation site-specific Nectin-4 targeting ADC



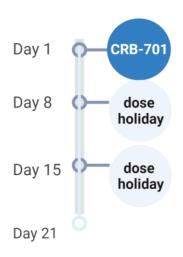


## **CRB-701:** One dose every 21 days expected to offer advantages over more frequent dosing

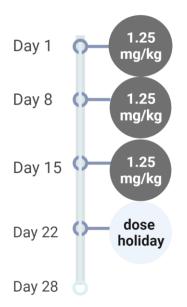


#### Clinical cycle comparison

**CRB-701** 



**Padcev**®





Patient / physician convenience

**Combination flexibility** 

#### Phase 1 dose escalation study (China): ASCO-GU 2024



#### **KEY ELIGIBILITY**

Age ≥18 years

Advanced urothelial

carcinoma or

Nectin-4 positive

Advanced solid tumors

ECOG 0-1

Adequate organ function

No uncontrolled diabetes

No active CNS metastasis

#### ESCALATION DESIGN

Bayesian Optimal Interval
(BOIN) design with
accelerated titration at DL-1
IV Q3W over a 21-day cycle
0.2 mg/kg
0.6 mg/kg
1.2 mg/kg
1.8 mg/kg
2.7 mg/kg
3.6 mg/kg

4.5mg/kg (recruiting)

#### KEY END POINTS

- Safety / tolerability
- Pharmacokinetics
- Anti tumor activity

#### NEXT STEPS

- Continue escalation
- PK expansion at 3.6mg/kg
- MTD or RP2D
- Specific expansion

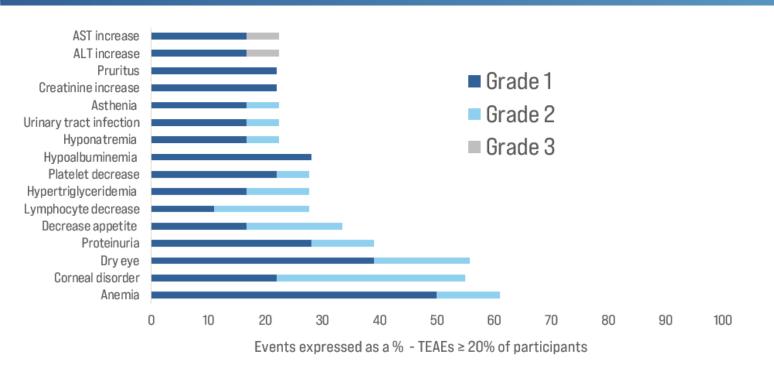
#### Demographics & Key Characteristics



Characteristic	Value	Characteristic	Value
Median Age (Range)	58 (35-76)	Primary tumor type	n=18
Sex (M/F)	5/13	Urothelial	7
ECOG PS of 1	18 (100%)	Cervical	6
Weight in kg (Range)	55 (36-84)	Breast	4
Prior therapy (Range)	5 (1-10)	TNBC	3 of 4
Creatine Cl <60 µmol/L	7 (39%)	CRC	1
Visceral metastasis	15 (83%)	HbA1C levels ≤ 6.5%	18 (100%)

#### Safety and Dose Modifications





Dose Modifications (n=18)	Value	
Discontinuations	0	
Reductions	0	
Interruptions	1(5.5%)	

- SYS6002 (CRB-701) was well tolerated with mainly grade 1 or 2 AEs
- No DLTs or Grade 4 or 5 AEs have been observed to date
- Anemia and eye-related adverse events were the most common treatment emergent AEs (TEAE)
- Four subjects reported 7 SAEs, 3 of which were considered probably related to SYS6002 (CRB-701)
   Two Grade 3 SAEs (ILD and pulmonary infection) were reported in a single participant
   One Grade 3 (ALT increase) reported in a separate participant
- To date no cases of skin rash or peripheral neuropathy have been observed

#### Clinical Pharmacology

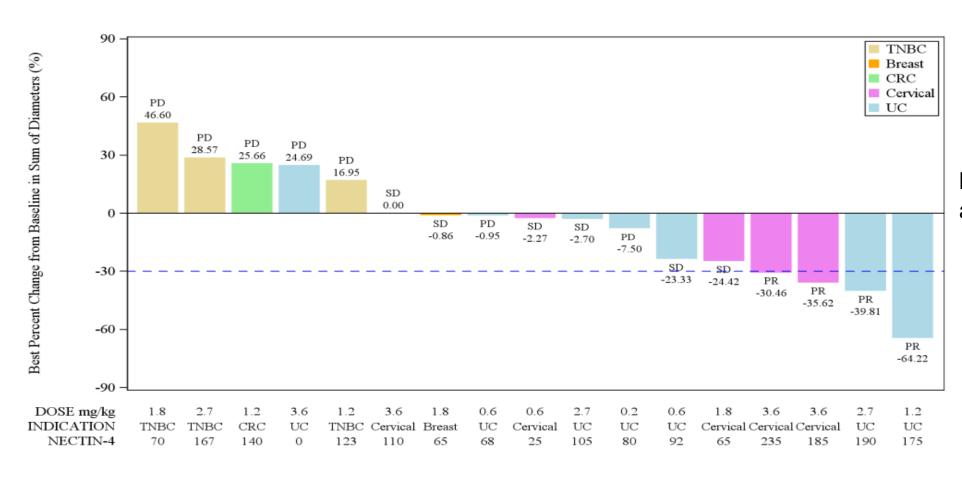


21 Day PK	Comparison	% ADC		% Free MMAE	
		Cmax	AUC 21d	Cmax	AUC 21d
Enfortumab vedotin (EV) 1.25 mg/kg Q1W x3	EV benchmark	100%	100%	100%	100%
SYS6002 (CRB-701) 1.2 mg/kg Q3W	Matched ADC dose	79%	106%	33%	29%
SYS6002 (CRB-701) 2.7 mg/kg Q3W	Matched MMAE dose	177%	183%	79%	68%

- After single IV infusion of SYS6002 (CRB-701), the exposure of TAb, ADC and MMAE generally increased in a dose proportional manner
- Clearance and volume of distribution were similar across doses
- The half-lives of TAb, ADC, and MMAE were 4-6 days, 4-5 days and 5-10 days, respectively
- No obvious accumulation was observed on C3D1
- Time-to-peak concentration of MMAE was about 3-7 days
- When compared to EV exposures SYS6002 (CRB-701) consistently demonstrates lower free MMAE

#### Phase 1 Dose Escalation - Disease Response





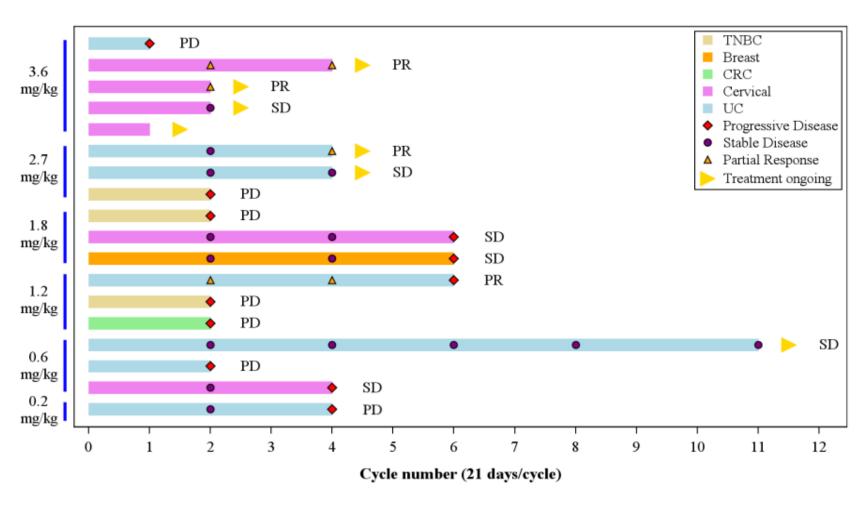
Disease response in 3.6 mg/kg and 2.7 mg/kg doses:

ORR 43%

DCR 71%

#### Phase 1 Disease Responses





Note: Of the 4 PRs reported, 2 PRs are confirmed and 2 remain unconfirmed

#### Phase 1 Summary - Data cutoff December 2023



Predicted therapeutically relevant doses in Ph. 1 study	Seven patients treated at 2.7mg/kg and 3.6 mg/kg on Q3W schedule
Objective Response Rate	43%: 3 out of 7 patients with PR's (2 unconfirmed)
Disease Control Rate	71%: 5 out of 7 patients
Tumor shrinkage across all nectin-4 positive mUC and cervical patients in study	9 out of 10 patients
Dose for first observed SD	0.6 mg/Kg
Dose for first observed PR	1.2 mg/Kg
Longest observed response duration to-date	11 cycles (still ongoing)
Participants still on CRB-701	7/18 (38%)
First expansion dose chosen	3.6 mg/Kg (cohort 6)

#### CRB-701: A differentiated clinical development approach to competitors



#### Proprietary insights are driving indication selection for CRB-701

mUC

New reality of Padcev® + Keytruda® 1L therapy

Under-served niche mUC populations remain and are attractive targets

Other Nectin-4 solid tumors

Emerging clinical data from current dose escalation is informative

Focus on unexplored Nectin-4 solid tumors

#### **CRB-701-01 Study Design (Corbus)**



Dose escalation (IND open: FPI Expected Q1 2024)

Project Optimus (dose optimization)

Dose expansion at RP2D

1.8 mg/Kg mg/Kg mg/Kg

Randomized to 2 doses of CRB-701 monotherapy

> Randomized to 2 doses of CRB-701+CPI

Bladder cancer niche population(s)

Non-UC tumors:

A

В

C

Basket of nectin-4 positive tumors

#### Validation of Nectin-4 as a Tumor Associated Antigen beyond mUC





PADCEV enfortunab vedotin-ejfv sensi in in disard dings \$8 mg/mil.





March 2024

15-	<- Other highly expressing tumors ->
10- 5-	

Elevated Nectin-4 expression: urothelial, breast, ovarian, cervical, colorectal, rectal, esophageal, gastric, lung,
thyroid, prostate, cholangiocarcinoma, pancreatic cancer, testicular cancer

Parameter	Patients (N=46)	Patients (N=37)
Confirmed ORR	11 (23.9%)	15 (40.5%)
CR	1(2.2%)	1(2.7%)
PR	10 (21.7%)	14 (37.9%)
DCR	26 (55%)	33 (89.2%)
PFS	3.94 months	Too early
Neutropenia (Grade 3+4)	4.3%	40%
Skin Rash	All grades: 45.7%	Grade 3+4: 17.5%
All grade 3+4 AEs	Not disclosed	70%

EV monotherapy 2019 FDA review (3)	Patients (N=310) 1.25mg/kg
Skin rash (grade 3+4)	10%
Any Grade 3-4 TEAE	58%

<sup>1.</sup> https://ascopubs.org/doi/abs/10.1200/JC0.2023.41.16\_suppl.6017

<sup>2.</sup> Efficacy and safety of 9MW2821, an antibody-drug conjugate targeting Nectin-4, monotherapy in patients with recurrent or metastatic cervical cancer: A multicenter, open-label, phase I/II study. SGO 2024 -source www.mabwell.com 3. NDA/BLA Multi-disciplinary review and Evaluation - BLA 761137

#### **Expected Milestones**



First patient dosed in U.S. dose escalation study	Q1-2024
Clinical data update on China dose escalation study	Mid-2024
Complete U.S. dose escalation study	Fall-2024
Present U.S. dose escalation data	Q4-2024/Q1-2025

#### CRB-701: Summary





Emerging clinical safety and potential for superior therapeutic index



Dose expansion has started (China); dose escalation in US Q1 2024



3<sup>rd</sup> generation ADC with improved linker stability-reduces MMAE in circulation

# CRB-913 Oral cannabinoid Type-1 inverse agonist for superior incretin therapy in obesity

## Incretin analogs have transformed the field of obesity and its commercial value



#### But...

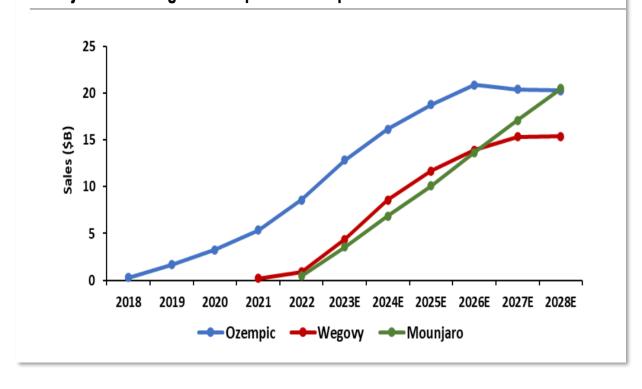
Muscle loss

**Tolerability** 

**Accessibility** 

→ Long-term compliance is ~ 27%

Sales (2018-2022) and sales estimates (2023-2028) for Ozempic, Wegovy, and Mounjaro reflect significant uptake and expectations



#### The obesity landscape is evolving to address these issues





Muscle loss: Degree of weight loss → Quality of weight loss



**Tolerability**: Single MOA → Multiple orthogonal MOAs

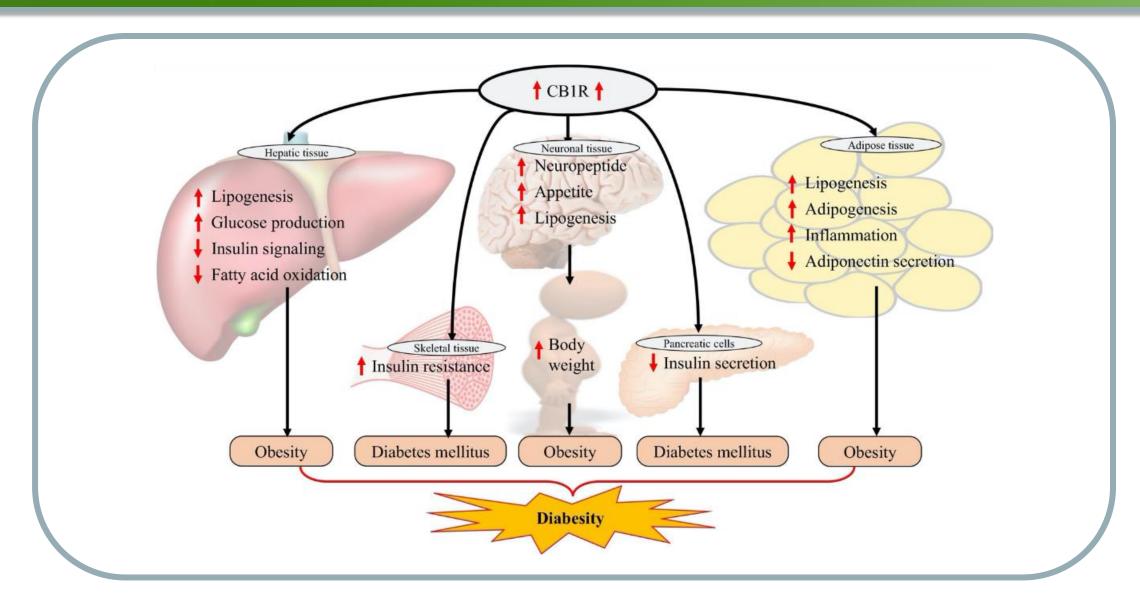


**Accessibility**: Injectables → Oral small molecules

# CB1 inverse agonism: The return of a clinically-validated obesity drug class

#### CB1 contribution to "Diabesity" is well understood





#### The CB1 MOA is clinically validated in obesity: data from 1st gen drugs

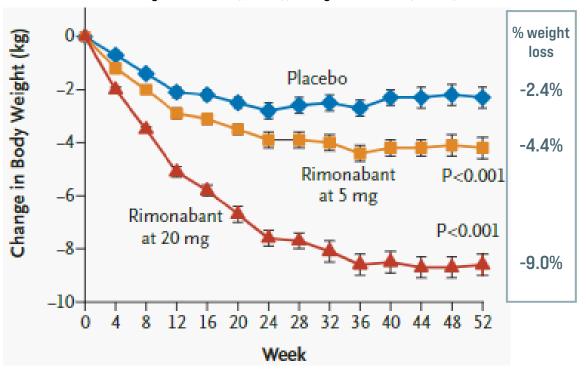


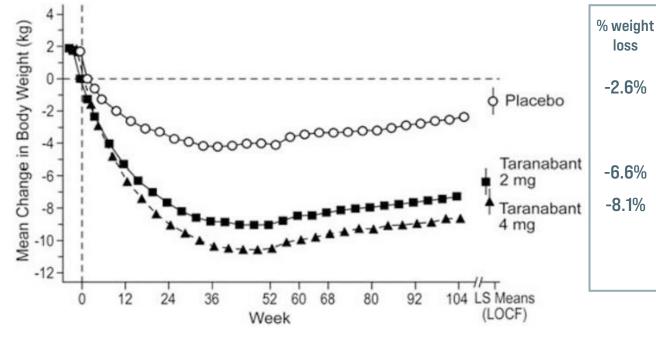


RIO-Lipids Phase 3 study
Placebo (n=342);
5 mg rimonabant (n=345); 20 mg rimonabant (n=346)



Completed Phase 3 studies (2 and 4 mg) (2 yr)
Placebo (n=417);
2 mg taranabant (n=414); 4 mg taranabant (n=415)





## Rimonabant weight loss was not associated with reduction of lean mass in obese patients



#### Phase 3 RIO study DEXA-scanned subgroup (n=146)

	Total body mass	Total fat mass	Fat mass/body mass	Lean mass
Rimonabant vs. placebo	<b>1</b>	<b>1</b>		Unchanged

Body composition was measured with body DEXA in a subset of patients in RIO Lipids. Decreases in the rimonabant 20 mg group relative to placebo were observed in the total body mass (p<0.001), the total body fat mass (p=0.001) and the fat mass/total body mass ratio (p=0.007). There was no statistically significant difference between the 20 mg and the placebo groups in lean mass loss between groups.

Rimonabant NDA (page 21)

## Muscle-CB1 K0 leads to increase in muscle mass in obese mice (Gonzalez-Mariscal et al, 2019)



Myotubes/Myofibers

## Muscle cannabinoid 1 receptor regulates II-6 and myostatin expression, governing physical performance and whole-body metabolism

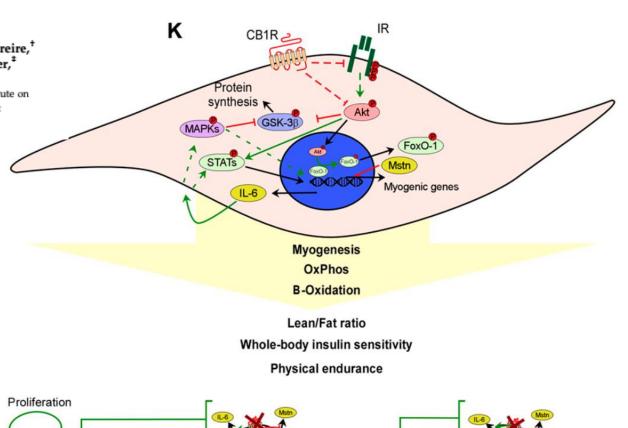
Isabel González-Mariscal,\*,¹ Rodrigo A. Montoro,\* Jennifer F. O'Connell,\* Yoo Kim,\* Marta Gonzalez-Freire,† Qing-Rong Liu,\* Irene Alfaras,† Olga D. Carlson,\* Elin Lehrmann,‡ Yongqing Zhang,‡ Kevin G. Becker,‡ Stéphan Hardivillé,§ Paritosh Ghosh,\* and Josephine M. Egan\*,²

\*Laboratory of Clinical Investigation, <sup>†</sup>Translational Gerontology Branch, and <sup>‡</sup>Laboratory of Genetics and Genomics, National Institute on Aging, National Institutes of Health, Bethesda, Maryland, USA; and <sup>§</sup>Unité de Recherche 8576–Unité de Glycobiologie Structurale et Fonctionelle (UGSF), Centre National de la Recherche (CNRS), Université Lille, Lille, France

#### Key finding:

Muscle-CB1K0 mice...

- Increase in muscle mass and strength
- Increase in biomarkers of muscle growth
- Increase in mitochondrial metabolism
- Increase in energy expenditure
- Increase in calorie consumption w/o weight gain
- Increase in fat metabolism
- Enhanced insulin sensitivity in muscle tissue
- Reduction in body fat content
- Reduction in sleep



Myocites

Differentiation

Myoblast

Myod

Fusion

and maturation

#### Next generation CB1 inverse agonists are peripherally restricted



#### **Next generation (2020 onwards)** First generation (2000-2007) Designed to target the brain with high BBB Designed to be peripherally restricted with minimal penetration → FDA rejection due to safety BBB penetration → avoid safety issues concerns (2007) INV-202 SANOFI 🧳 Rimonabant CRB-913 **Otenabant** Bristol Myers Squibb **Ibipinabant Taranabant**

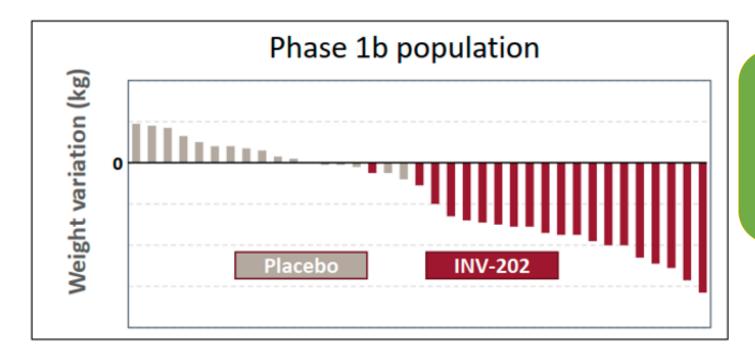
#### Novo Nordisk acquisition of Inversago marks return of CB1 as an MOA in obesity



Novo acquires Inversago for up to \$1 billion, spotlighting troubled weight loss

approach

Aug. 10, 2023



- Single-dose INV-202 (25mg QD)
- 2. N = 37
- 3. Adults with metabolic syndrome
- 4. Weight loss: -3.50 kg (INV-202) vs +0.55Kg (placebo)

### CRB-913: oral CB1 inverse agonist for combination therapy with incretins

**OBESITY SYMPOSIUM** 

Novel cannabinoid receptor 1 inverse agonist CRB-913 enhances efficacy of tirzepatide, semaglutide, and liraglutide in the diet-induced obesity mouse model

Obesity OBESITY WILEY

Nov. 2023





#### Design Goals

- Best-in-class peripheral restriction
- Protect lean mass (muscle)
- Retain 1<sup>st</sup> gen efficacy
- **Enhance efficacy of incretin analogs**

#### CRB-913 is the outcome of a multi-year medicinal chemistry campaign



CRB-913

Ibipinabant (2004-2008)

JD-5037 (2012-2018) / CRB-4001 (2018-2021)

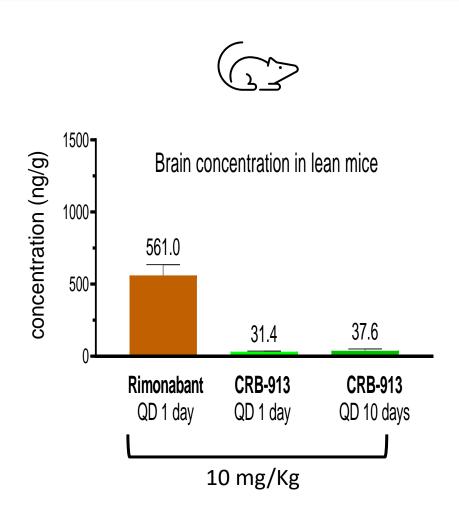
- Completed Phase IIb (Solvay/BMS)
- Small, lipid soluble molecule
- High BBB penetration
- Oral

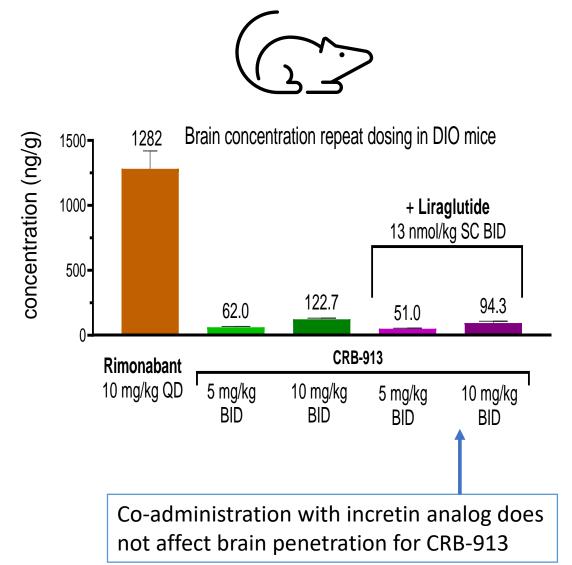
- CRB-4001 (JD5037) licensed from Jenrin in 2018
- Extensive pre-IND studies carried out
- PK didn't support TPP
- Oral

- New IP published patent coverage through 2043
- PK profile optimized for TPP
- Favorable multi-species bioavailability (>50%)
- Lower mfg. cost vs. incretins
- Oral

#### CRB-913: marked peripheral restriction vs. rimonabant in both lean and obese mice







#### CRB-913: higher degree of peripheral restriction than INV-202

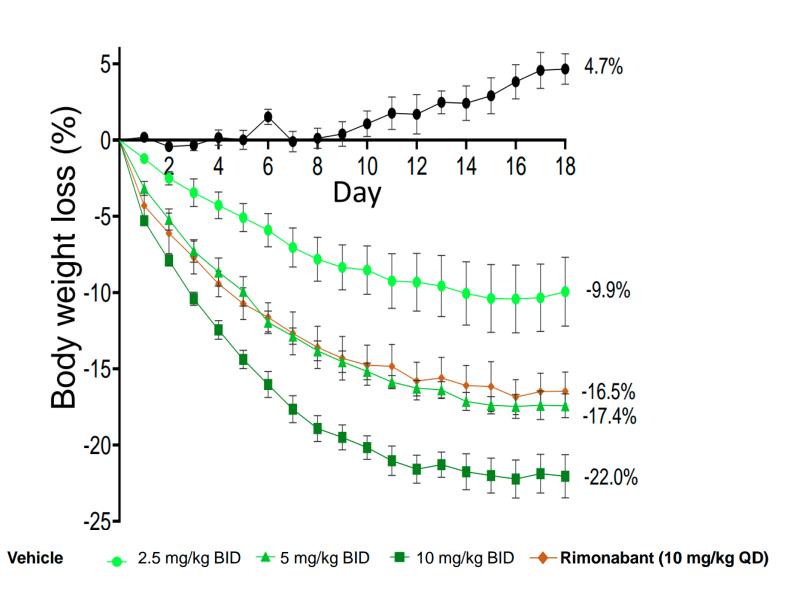


Brain concentration (ng/g)					
single acute dose	CRB-913 (lean mice)	INV-202 (lean mice)	Rimonabant (lean mice)		
10 mg/Kg	26*	319**	561*		

1:12

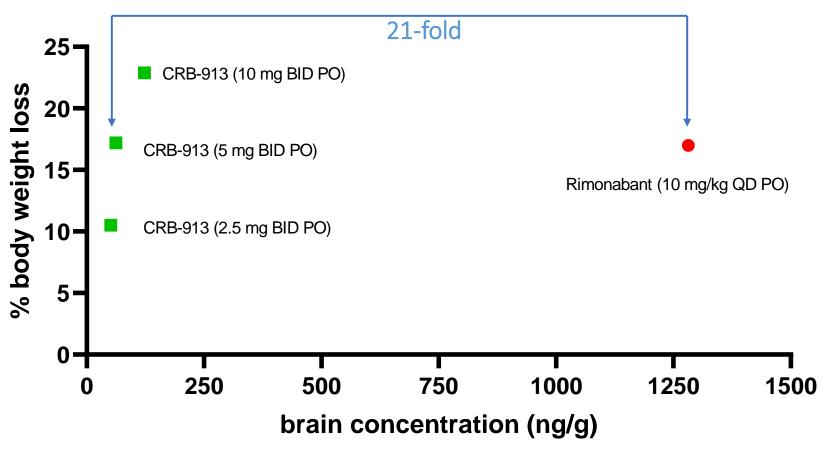
#### CRB-913: similar weight loss vs. rimonabant at same daily doses in DIO mice







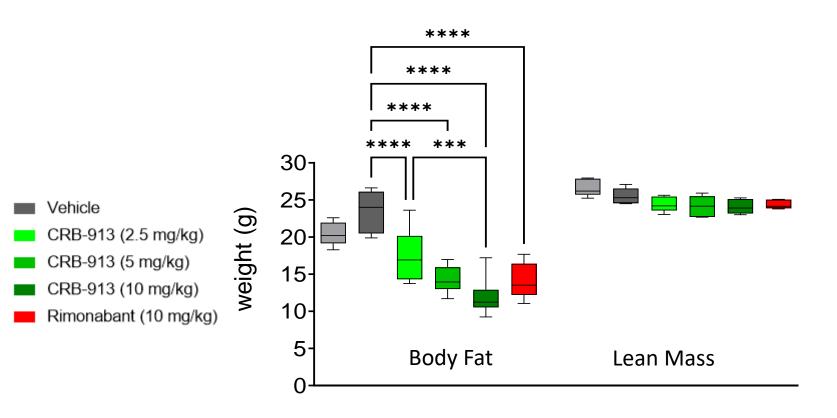




- DIO mouse model with C57BL6/N mice (n=10) fed a continuous high fat diet for 22 weeks prior and during 28 days of treatment
- Brain collected 1 h post final dose (C<sub>max</sub>)

#### CRB-913 demonstrates significant reduction in body fat content but not lean mass

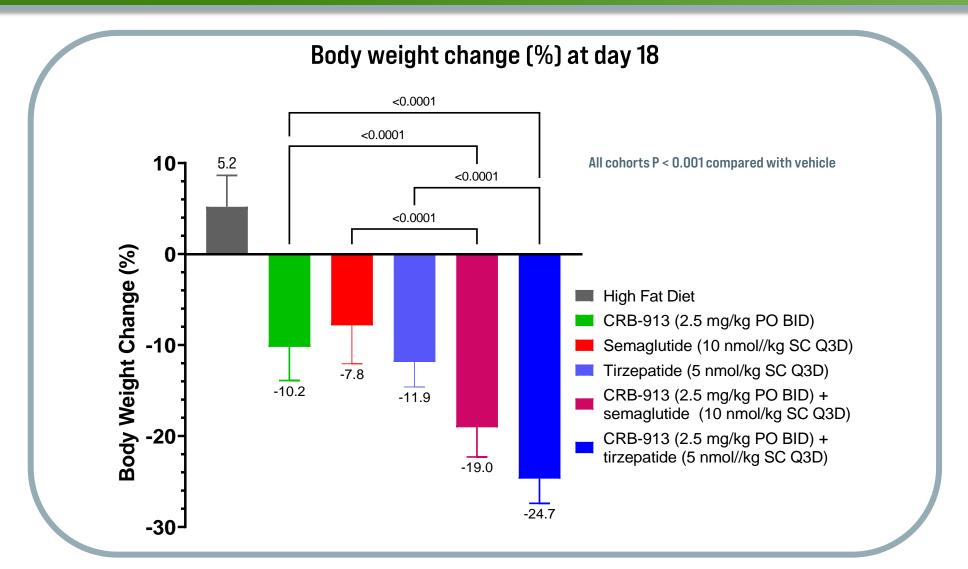




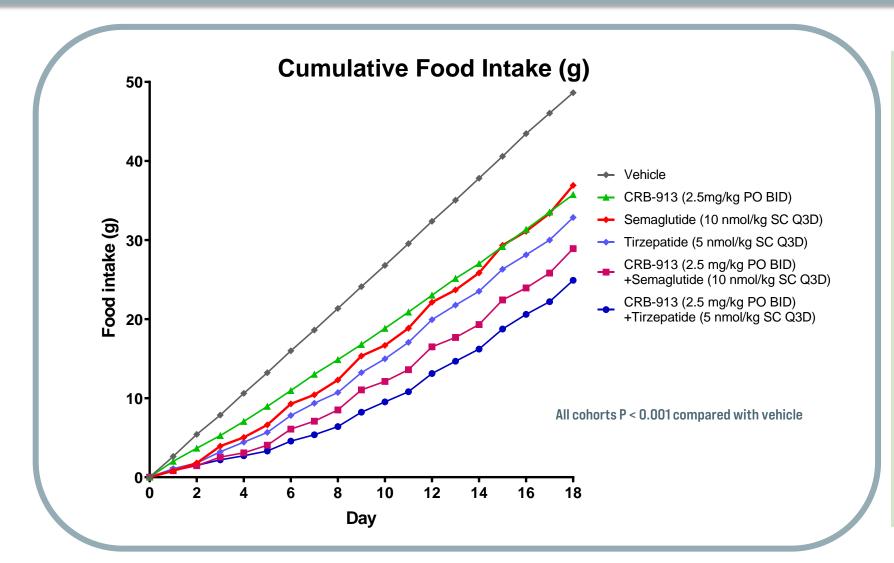
- DIO mouse model with C57BL6/J mice (n=10) fed a continuous high fat diet for 22 weeks prior
  - Body fat by MRI determined on Day 20

#### CRB-913: enhanced combo effect with semaglutide or tirzepatide







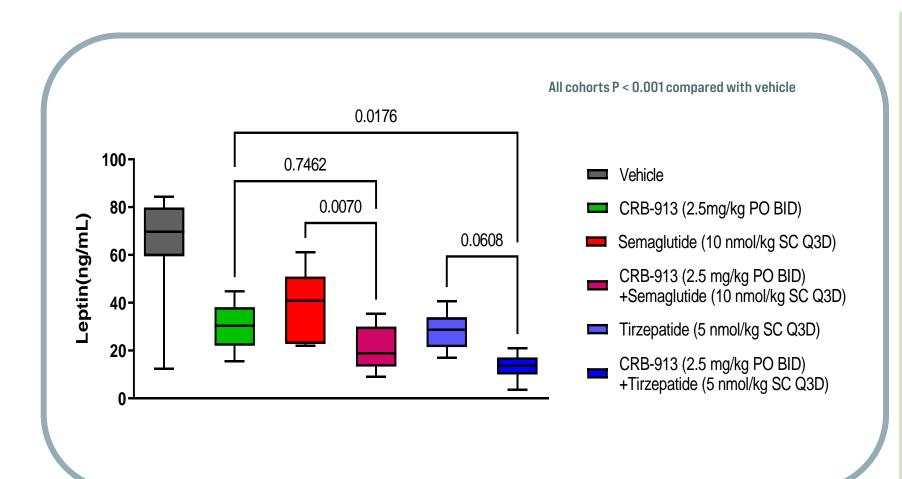


#### **Food Consumption**

- CRB-913, semaglutide and tirzepatide each results in food intake reductions
- Significant further reductions in food consumption when CRB-913 is combined with semaglutide or tirzepatide (p=0.001)

#### CRB-913 reverses leptinemia alone and in combination with semaglutide or tirzepatide





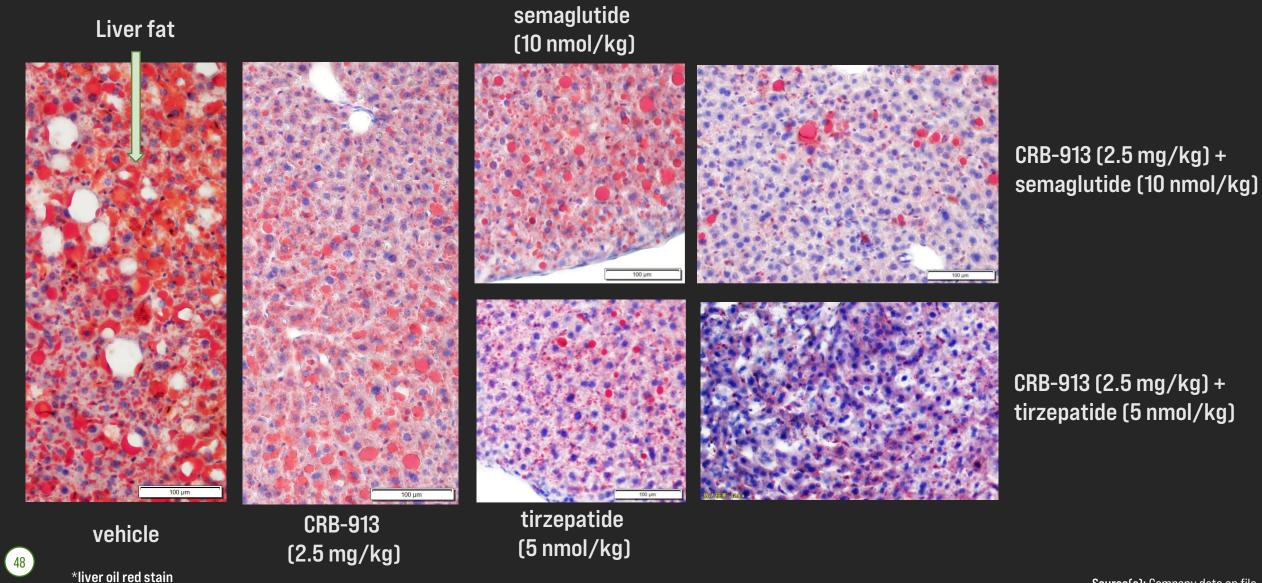
#### The Role of Leptin

- The hormone leptin regulates food intake
- Normally, leptin signals satiety (feeling "full")
- In obesity, resistance to leptin
  develops and hunger persists despite
  high leptin levels ("leptinemia")
- A reduction in leptin levels is believed to be important for weight loss<sup>1</sup>

- DIO mouse model with C57BL6/J mice (n=10) fed a continuous high fat diet for 22 weeks prior
- Leptin measured at Day 28 of treatment

#### CRB-913 reduces liver fat alone and in combination with semaglutide or tirzepatide





#### CRB-913: Clinical development pathway and potential clinical usage





#### Potential clinical applications:



Incretin analog therapy insensitive/intolerant/high-risk patients



Combination with oral incretin agonists  $\rightarrow$  enhance efficacy OR improve tolerability



"Induction/maintenance" model: maintain weight loss post incretin analog therapy

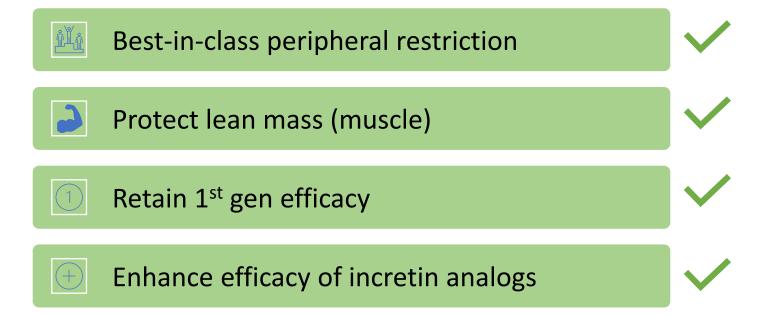
#### **Expected Milestones**



Produce drug for toxicology and clinical studies	Q2-2024
Complete toxicology and IND enabling studies	Q3-2024
File IND	Q4-2024
Dose first patient	Early 2025

#### CRB-913: designed to be a best-in-class next gen CB1 inverse agonist





# Leadership Upcoming catalyst Financials

#### Management Team





Yuval Cohen, PhD Chief Executive Officer, Director

Corbus co-founder and Chief Executive Officer since 2014. Previously the President and co-founder of Celsus Therapeutics from 2005.



Dominic Smethurst, PhD Chief Medical Officer, MA MRCP

Dr. Smethurst, MA MRCP, joined Corbus as our Chief Medical Officer in February 2024. He most recently served as CMO of Bicycle Therapeutics.



Sean Moran, CPA, MBA Chief Financial Officer

Corbus co-founder and Chief Financial Officer since 2014. Prior senior financial management experience in emerging biotech and medical device companies.



Christina Bertsch Head of Human Resources

Accomplished senior human resource executive providing strategic HR consulting services to both large and small businesses across a variety of industries.

#### **Board of Directors**





Amb. Alan Holmer Ret. Chairman of the Board

More than two decades of public service in Washington, D.C. including Special Envoy to China; Former CEO of PhRMA.



Rachelle Jacques
Director

More than 25-year professional career, experience in U.S. and global biopharmaceutical commercial leadership, including multiple high-profile product launches in rare diseases; CEO of Akari Therapeutics. (NASDAQ: AKTX)



Anne Altmeyer, PhD, MBA, MPH Director

20 years of experience advancing oncology R&D programs and leading impactful corporate development transactions; currently President & CEO of TigaTx.



John K. Jenkins, MD
Director

Distinguished 25-year career serving at the U.S. FDA, including 15 years of senior leadership in CDER and OND.



Avery W. (Chip) Catlin
Director

More than 25 years of senior financial leadership experience in life science companies; Former CFO and Secretary of Celldex Therapeutics.



Pete Salzmann, MD, MBA

Director

20 years of industry experience and currently serves as Chief Executive Officer of Immunovant (NASDAQ: IMVT), a biopharmaceutical company focused on developing therapies for patients with autoimmune diseases.



Yuval Cohen, PhD
Chief Executive Officer, Director

Corbus co-founder and Chief Executive Officer since 2014. Previously the President and co-founder of Celsus Therapeutics from 2005.



Yong (Ben) Ben, MD, MBA Director

25 years of oncology R&D experience across industry and academia. Held two industry CMO positions, most recently at BeiGene (BGNE).

#### **Expected Corporate Milestones**



**CRB-701** 

First patient dosed in U.S. dose escalation study: Q1-2024

Clinical data update on China dose escalation study: Mid-2024

Complete U.S. dose escalation study: Fall-2024

Present U.S. dose escalation data: Q4-2024 / Q1-2025

**CRB-913** 

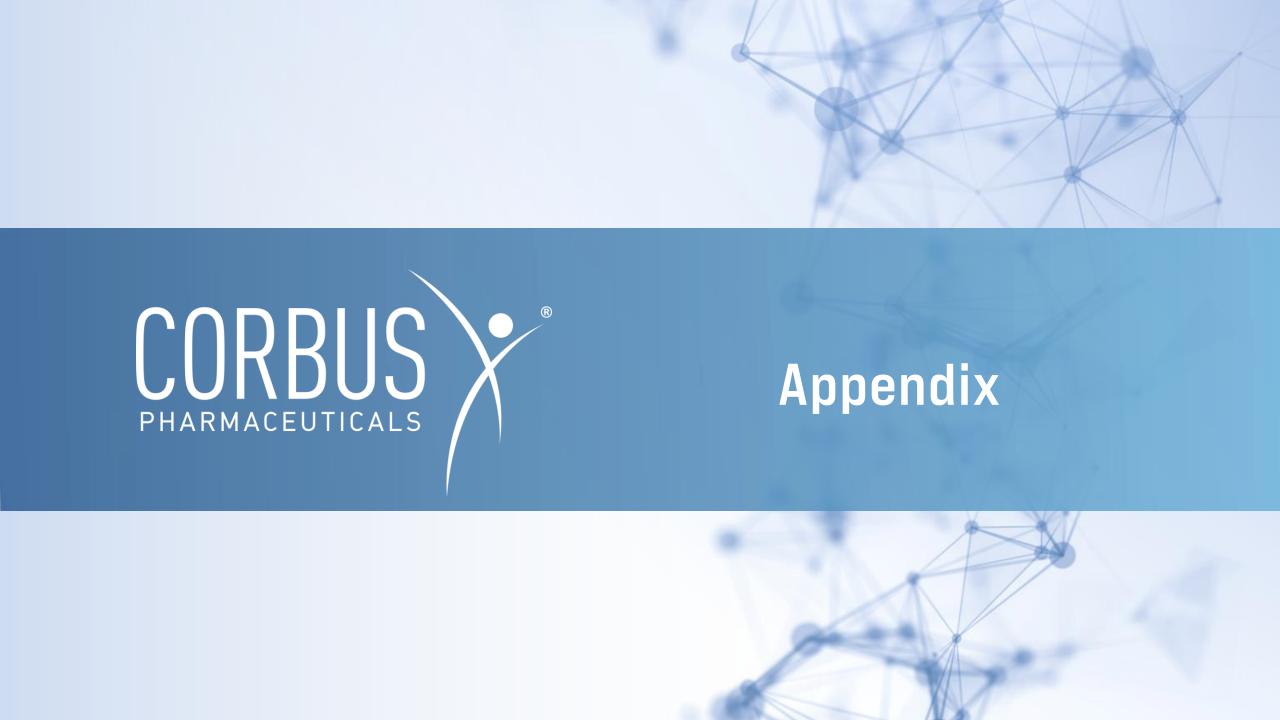
File IND: Q4-2024

First patient dosed: early 2025

**CRB-601** 

IND cleared: January-2024 ✓

First patient dosed: Summer 2024



## $\begin{array}{l} \text{CRB-601} \\ \text{Potential "best-in-class"} \\ \alpha v \beta 8 \text{ mAb} \end{array}$

#### CRB-601 has the potential to enhance checkpoint inhibition





Novel mechanism to target  $TGF\beta$  in the tumor microenvironment



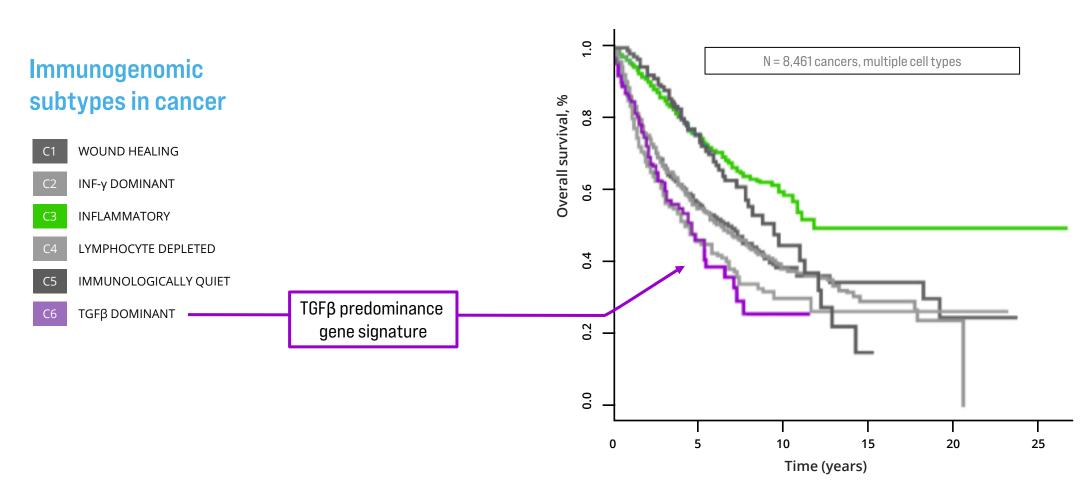
Focus on adopting a precision-targeted approach



Large opportunity potential if POC is validated

#### TGFβ predicts poor clinical outcomes in a subset of cancer patients





Gene expression, immune cell quantification & network mapping

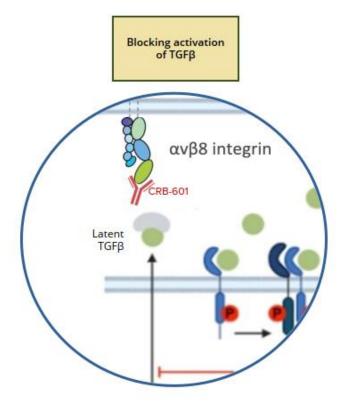
• 33 different cancer types / 8,000+ tumors

#### Targeting the integrin $\alpha v\beta 8$ represents a novel approach to regulating TGF $\beta$

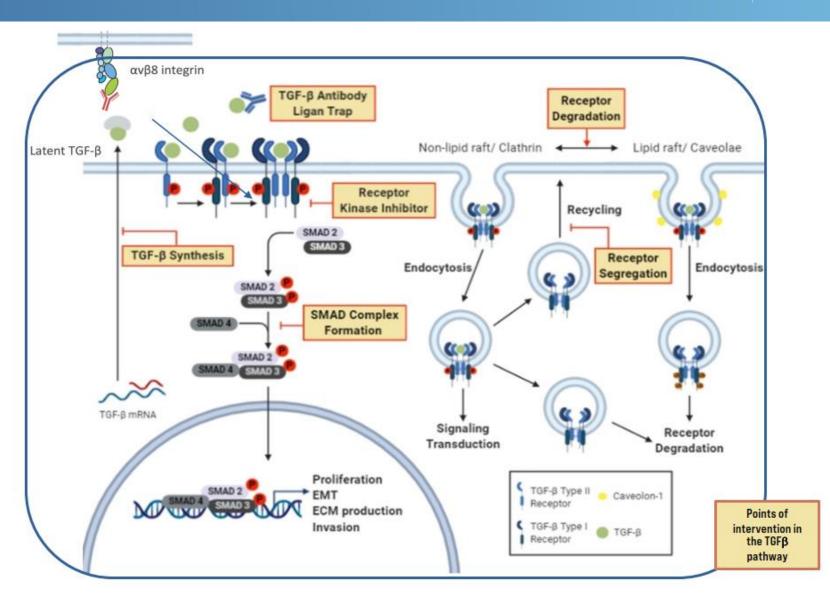


#### Novel point of therapeutic intervention

Blocking the ανβ8 activation of TGFβ in the local tumor microenvironment



CRB-601 binds at the interface between latent TGF $\beta$  and  $\alpha v \beta 8$ 



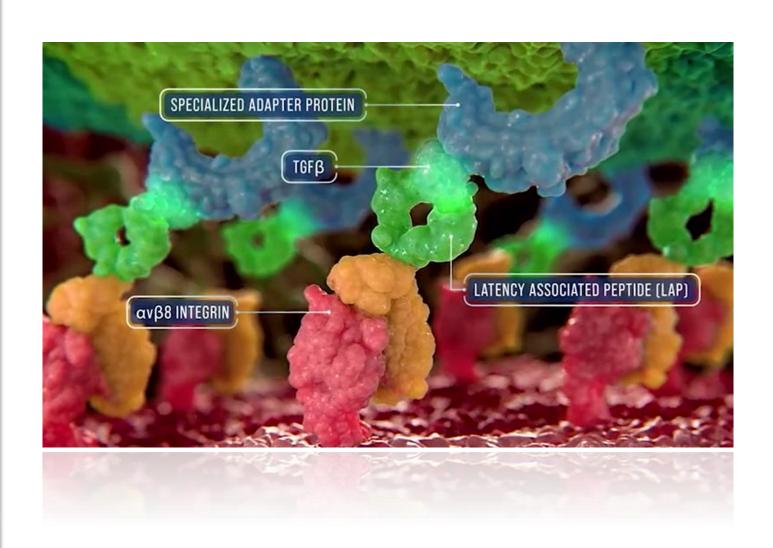
#### CRB-601 is targeting latent -TGF $\beta$ by blocking the integrin $\alpha v \beta 8$



The integrin  $\alpha v\beta 8$  is expressed in the tumor microenvironment (TME)

Latent-TGFβ is also expressed in the TME

CRB-601 is a blocking antibody preventing the interaction of these two proteins



#### mAbs targeting TGFβ activation are advancing clinically









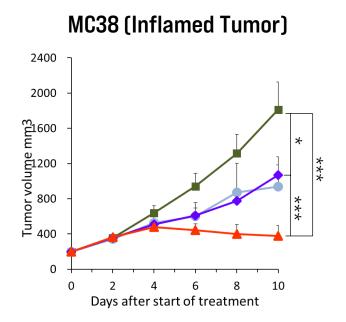




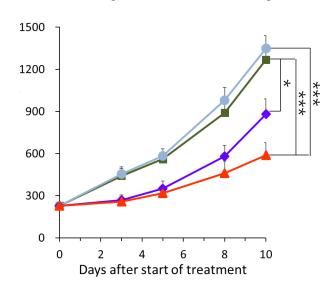
	CRB-601	PF-06940434	SRK-181	ABBV-151	RG6440
MOA	ανβ8	ανβ8	L-TGFβ	GARP (TGFβ1)	L-TGFβ
Clinical Stage	IND Cleared Jan 24	Phase 1/2	Phase 1	Phase 2	Phase 1
Indications	Solid Tumors	Solid Tumors	Solid Tumors	HCC Updated 11/23	Solid Tumors
Туре	Monoclonal Antibody	Monoclonal Antibody	Monoclonal Antibody	Monoclonal Antibody	Monoclonal Antibody
ROA	IV	IV	IV	IV	IV

#### CRB-601 enhances anti-PD-1 therapy in checkpoint inhibition sensitive and resistant murine tumor models

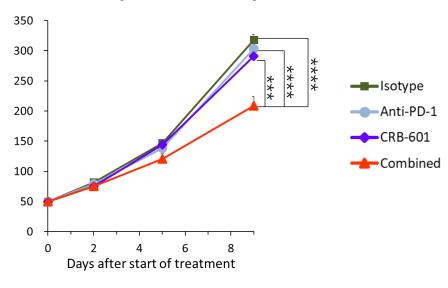




#### **EMT6 (Excluded Tumor)**



4T1 (Desert Tumor)



#### **Checkpoint blockade sensitivity**

#### Sensitive

% TGI	MC38	ЕМТ6	4T1
Anti-PD-1	54	-8	6
CRB-601	46	37	10
Combo	89	65	41

Resistant

CRB-601: 10 mg/kg BIW

Anti-PD-1: 10 mg/kg BIW

10 animals / group

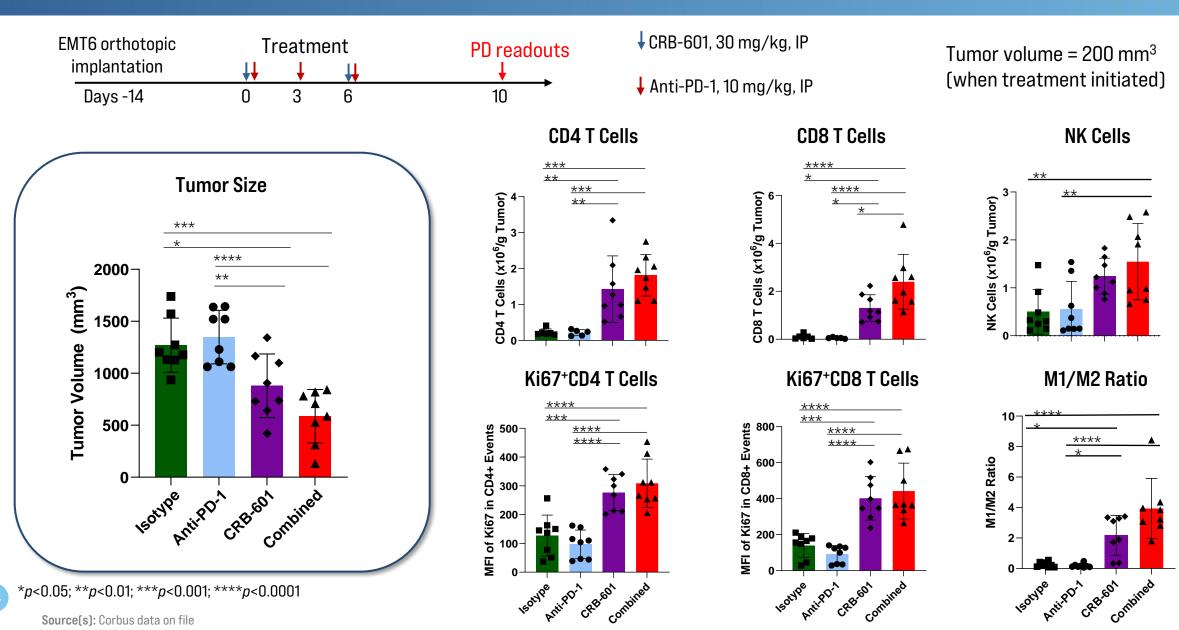
Animals randomized at 50-80 mm<sup>3</sup>

Comparisons across arms

63

#### Blockade of $\alpha v\beta 8$ in combination with anti-PD-1 increased TIL populations in immune excluded EMT6 tumors





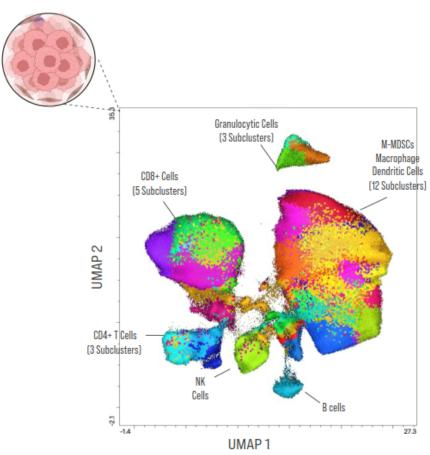
#### CRB-601 reshapes the landscape of effector T and NK cells in MC38 tumors



Isotype

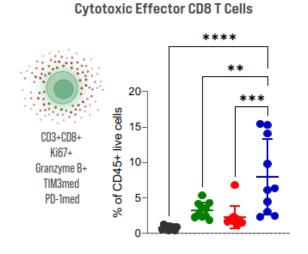
CRB-601

Combination



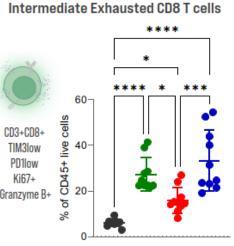


- 1.25 million live CD45+ cells analyzed
- 31 immune clusters from high dimensional flow analysis
- . Sample processing (1) Downsample (2) UMAP (3) X-Sift (4) Euclid (5) Cluster Explorer
- · Animals have undergone 10 days of treatment.

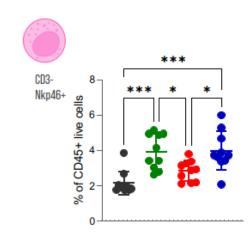


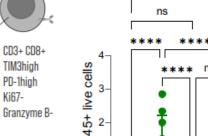
Terminally Exhausted CD8 T cells

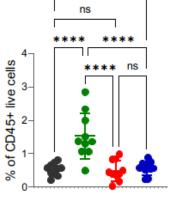
#### cells <u>Xe</u> CD45+ Granzyme B+



**Natural Killer Cells** 







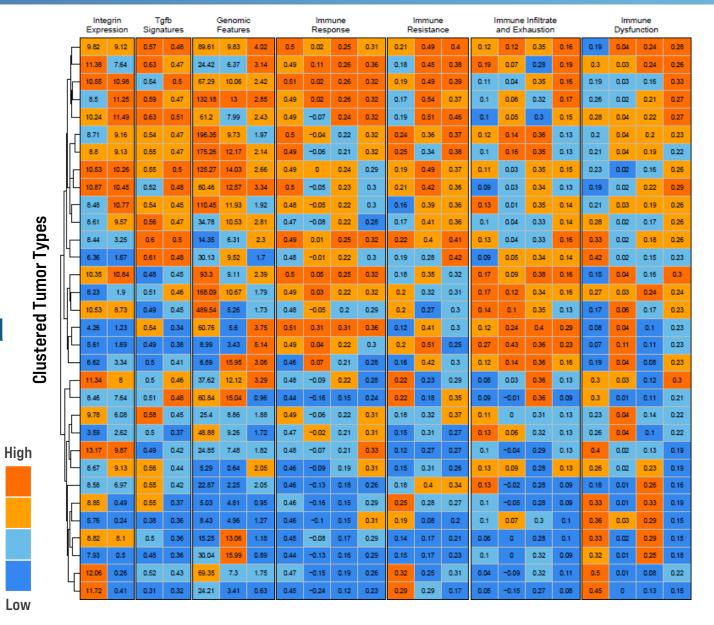
#### Applying a proprietary algorithm to define the clinical focus for CRB-601

Quartiles



A multi-parametric, immune-focused algorithm has refined indications for CRB-601

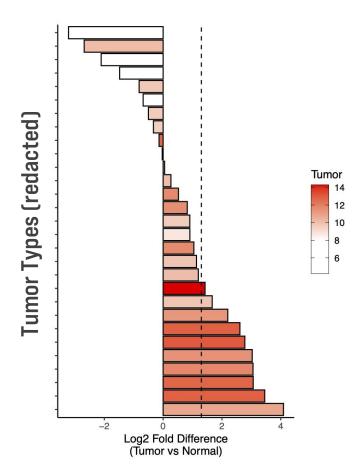
The combination of immune features and gene expression profiles have identified 9 indications for clinical priority

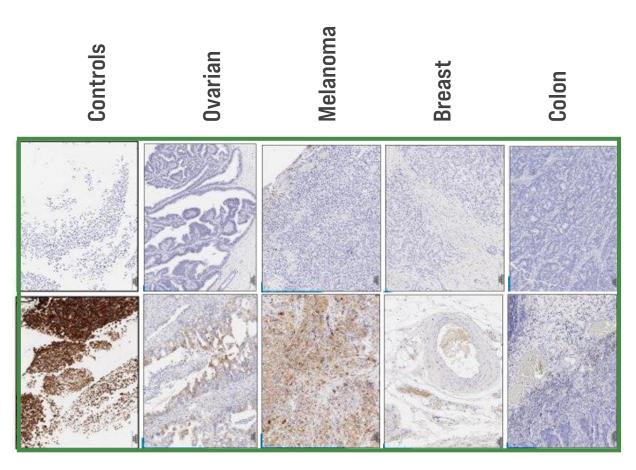


#### Patient selection strategies will enhance the probability of success



Prioritization of indications with differential gene expression vs. normal tissues will emphasize focus on the tumor potential of  $\alpha v \beta 8$ 





Development of a NEW patient enrichment biomarker will assist in enriching for responses and addressing the right immune resistant patient population with CRB-601

#### **Expected Milestones**



IND cleared	January 2024
First patient dosed	Summer 2024
Dose escalation and confirmation	2 <sup>nd</sup> Half of 2024