

### **Crescent Biopharma Overview**

November 2024

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### **Crescent Biopharma aims to advance the next wave of innovation in cancer therapy**

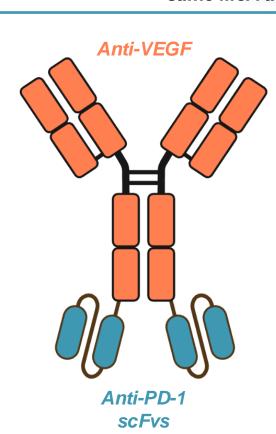
Crescent's pipeline consists of potentially best-in-class therapies for the treatment of solid tumors.

- Crescent is the fifth company launched with assets discovered and in-house by Paragon Therapeutics, a leading biotech incubator founded by Fairmount Funds in 2021.
  - Prior companies founded with Paragon assets have collectively raised >\$2B and generated significant value.
- ~\$200 million financing in October 2024 anticipated to fund operations through 2027.

Program	МоА	Stage			Potential
		Discovery	IND- enabling	Clinical	Indications
CR-001 <sup>1</sup>	<b>PD-1 x VEGF</b> (same cooperative MoA as ivonescimab)			YE25 / 1Q26	NSCLC, other solid tumors
CR-002	<b>Undisclosed #1</b> (ADC, Topol payload)			Mid-26	Solid tumors
CR-003	<b>Undisclosed #2</b> (ADC, Topol payload)				Solid tumors



### **Crescent is advancing three highly impactful oncology programs** with best-in-class potential



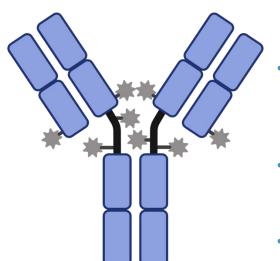
 Designed to reproduce ivonescimab's established pharmacology.

**CR-001** 

PD-1 x VEGF cooperative tetravalent bsAb;

same MoA as ivonescimab

- Pipeline in a program opportunity across solid tumor indications, with potential to move to frontline use in the \$50B+ PD-(L)1 immunotherapy market.
- IND expected YE25 / 1Q26.
- Interim PoC data expected 2H26.



Two unique, undisclosed targets with **significant potential across solid tumors** as single agents.

CR-002 & CR-003

ADCs with topoisomerase inhibitor payloads;

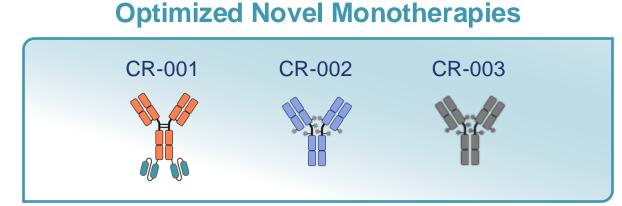
potentially best-in-class

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- Each has potential to synergize with CR-001 in combination studies, further driving clinical efficacy.
- Both utilize the best-inmodality cytotoxic payload: topoisomerase inhibitor.
- CR-002 IND expected mid-26.
- Interim PoC data expected in 2027.



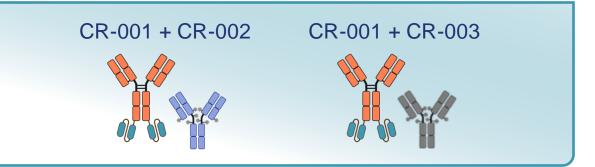
# Multiple ways to win: Crescent pipeline enables optionality with differentiating combination therapies



#### **Engineered for:**

Best-in class efficacy	Safety
Efficacy across solid tumors	Stability
Pharmacokinetics	Developability

#### **Synergistic Combination Approaches**



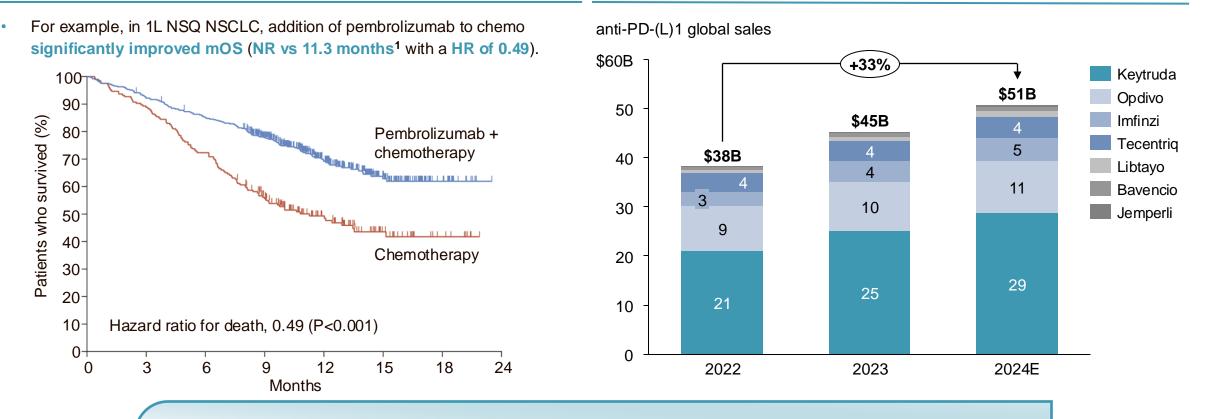
#### **Selected for:**

Mechanism of action synergy Efficacy in overlapping solid tumors Broad utility



# PD-(L)1-targeted therapies, annualizing \$50B+, have transformed oncology – with Keytruda now the best-selling drug in the world

PD-(L)1 inhibitors have significantly prolonged survival, shifting 1L treatment to immunotherapy PD-(L)1-targeted therapies are one of the largest drug classes, with Keytruda (pembrolizumab) the dominant player



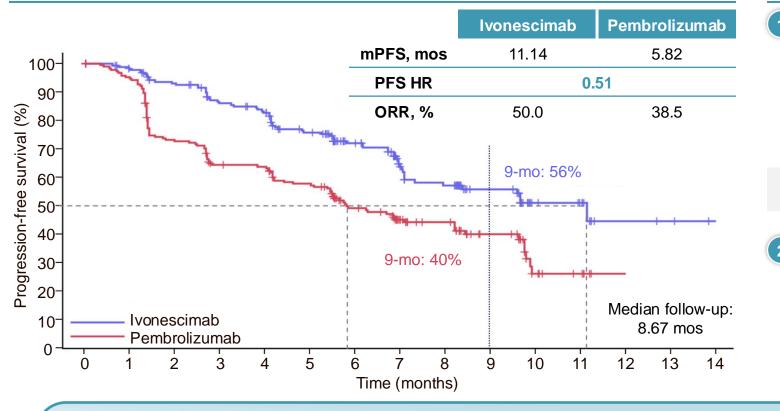
Keytruda alone is approved in 20+ oncology indications with expected revenue of ~\$30B in 2024.



Notes: 1. 5-year follow up demonstrated mOS of 22.0 vs 10.6 months. NSQ: Non-squamous. NSCLC: Non-small cell lung cancer. mOS: median overall survival. Sources: 2018 Gandhi (NEJM); 2023 Garassino (J Clin Oncol); GlobalData; FactSet; Pembrolizumab FDA Label

# Ivonescimab, a cooperative PD-1 x VEGF bispecific, doubled progression-free survival vs. Keytruda in a P3 NSCLC trial

Ivonescimab is the first drug to demonstrate <u>superiority</u> in PFS over pembrolizumab in a randomized Phase 3



#### Ivonescimab's novel MoA raises the bar on efficacy and safety

**Broader efficacy**: Ivonescimab demonstrates benefit in patients where anti-PD-(L)1 efficacy has historically been modest (e.g., squamous, PD-(L)1<sup>low</sup>).

	PD-L1 <sup>low</sup> ( <i>TPS 1-49%</i> )	PD-L1 <sup>high</sup> ( <i>TPS</i> ≥50%)	Non- squamous	Squamous
HR	0.54	0.46	0.54	0.48

Promising safety: Ivonescimab had lower AEs than expected versus anti-VEGF monotherapy. This suggests a differentiated profile driven by cooperativity-driven tissue targeting.

Dual blockade of PD-1 and VEGF through a cooperative bispecific antibody has led to unprecedented clinical results, demonstrating superiority to pembrolizumab... and a \$15B+ market cap for ivo's ex-China sponsor, Summit Therapeutics.



Notes: HR: hazard ratio. PFS: progression-free survival. AE: adverse event. NSQ: Non-squamous SQ: Squamous. Akeso has licensed ivonescimab to Summit in North America, South America, Europe, Africa, Middle East, and Japan. Akeso maintains rights in Asia (ex-Japan / Middle East) and in Oceania. Sources: 2024 Zhou (WCLC Presentation on HARMONi-2); Summit Therapeutics; 2018 Paz-Area (NEJM); 2019 Mok (Lancet); 2022 De Castro Jr (J Clin Oncol); Avastin Label

### **CR-001**

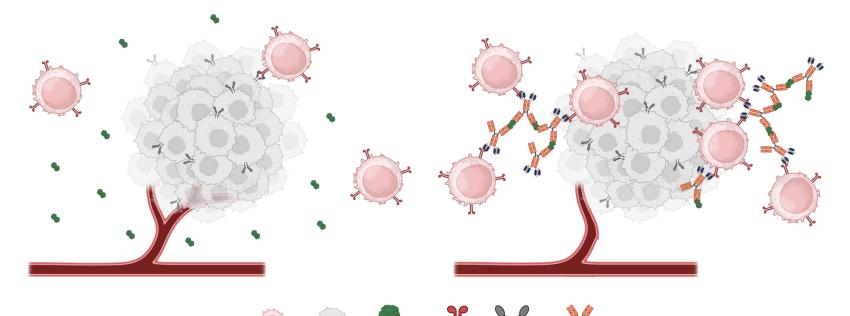
Cooperative, tetravalent PD-1 x VEGF bispecific antibody

### Ivonescimab's novel, cooperative MoA hypothesized to drive enhanced anti-tumor activity while maintaining tolerability

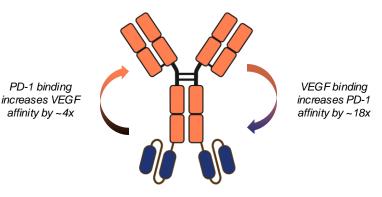
VEGF drives tumor angiogenesis and PD-L1 expression suppresses T cells



lvo's cooperative binding blocks PD-1 / PD-L1 interactions and inhibits VEGF



Cooperativity: VEGF binding to ivonescimab increases affinity to PD-1 and vice versa, enhancing both T-cell activation and VEGF-signaling blockade. This helps explain the cross-trial outperformance of ivonescimab vs. an anti-PD-L1 + anti-VEGF combination.



✓Tumor targeting: PD-1 arm concentrates VEGF inhibition in the TME, potentially sparing healthy tissue and reducing AEs.

Dual blockade of PD-1 and VEGF through a novel tetravalent bispecific format with cooperative binding effects has led to unprecedented clinical results in third party trials.

PD-L1 Ivonescimab



Tumo

cell

VEGF

dimer

PD-1

T cell

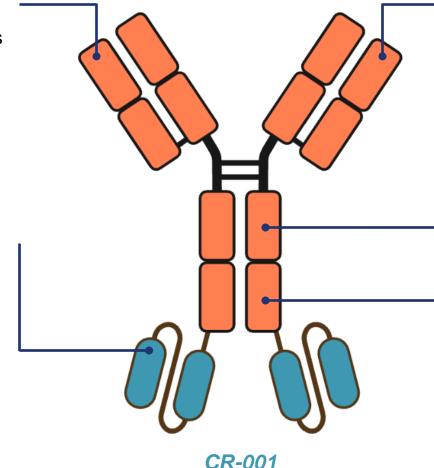
# CR-001 is a highly potent PD-1 x VEGF bsAb designed to recapitulate ivonescimab's cooperative pharmacology

#### Same design as ivonescimab

- Pairs anti-VEGF IgG & anti-PD-1 scFvs
- Avoids risk of alternative, clinically unprecedented constructs (e.g., VEGF trap, anti-PD-L1 IgG, ADCC)

#### Highly potent & stable scFvs

- Designed to be the <u>best possible</u> anti-PD-1 epitope / binding domain
- Anti-PD-1s have historically outperformed anti-PD-L1s in metaanalyses of solid tumor studies
- Contains proprietary engineering to enable functional and stable scFvs



#### **Potential for reduced AEs**

- Cooperative binding increases anti-VEGF activity in TME, reducing AE risks in healthy tissue
- Identical VEGF potency to preserve safety

#### Effector-null human IgG Fc

- Equivalent to ivonescimab
- ADCC carries additional AE risk

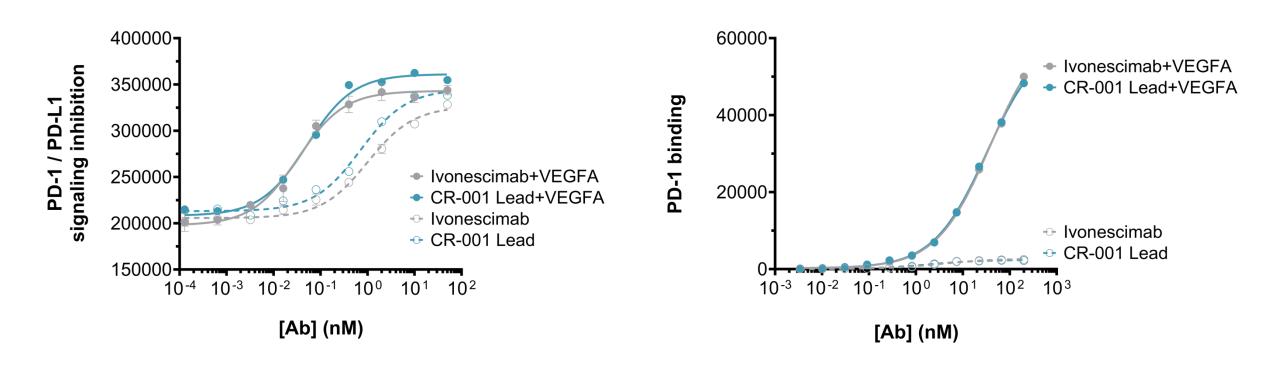
#### **Designed to match ivonescimab PK**

 Native FcRn binding to match distribution and elimination of ivonescimab



# CR-001 replicates ivonescimab's cooperative effect, with greater binding to and inhibition of PD-1 signaling in presence of VEGF

CR-001 lead, like ivonescimab, is more potent in an NFAT reporter assay in the presence of VEGF... ... and also increases PD-1 binding on PD-1+ Jurkat cells in the presence of VEGF.



CR-001 lead demonstrates same cooperative effect as ivonescimab across multiple assays.

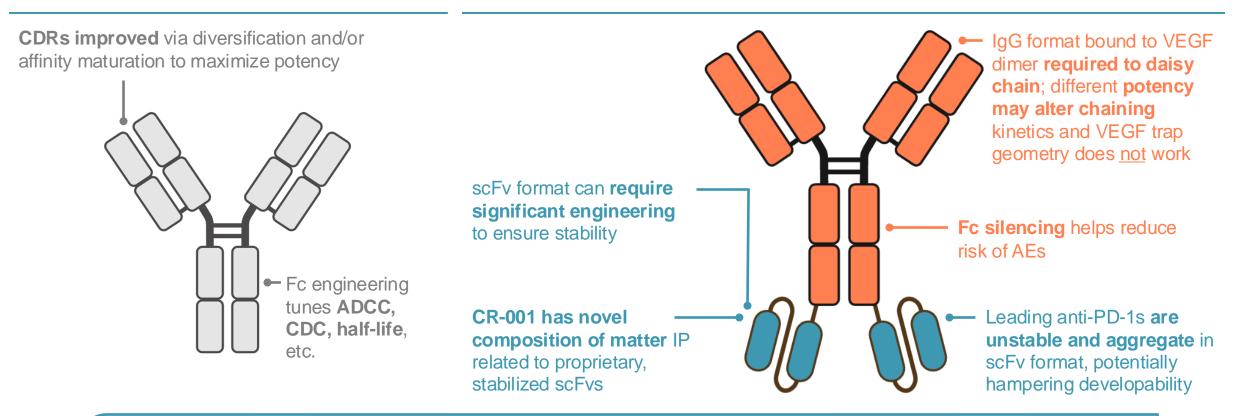


Notes: Ivonescimab generated internally based on published sequence. PD-1 / PD-L1 signaling inhibition measured in RLU (relative light units), a measure of luminescence that increases with greater inhibition. PD-1 binding measured in MFI (mean fluorescence intensity), a measure of fluorescence that increases with binding and is measured via FACS. Sources: Internal data

# Replicating ivonescimab's tetravalent format and cooperativity, with stable scFvs, requires complex protein engineering

Standard mAbs can be improved with established protein engineering approaches...

... but ensuring cooperative effect, stability, and developability of tetravalent PD-(L)1 x VEGF bispecific antibody is more difficult



Ivonescimab's unique structure and geometry – and resulting cooperative function – is challenging to replicate; alternative constructs risk not reproducing ivonescimab's superior efficacy and safety in clinical practice.



### CR-001 has potential to transform SoC across a multitude of oncology indications, with numerous first-in-class opportunities

#### SOFT TISSUE

- Alveolar soft part sarcoma
- Soft tissue sarcoma

#### **HEMATOLOGICAL**

- Classical Hodgkin lymphoma
- Primary mediastinal large B-cell lymphoma (PMBCL)

REPRODUCTIVE

- Cervical
- Endometrial
- Fallopian tube
- Ovarian (epithelial)
- Triple negative breast cancer (TNBC)
  - Urothelial



BRAIN Glioblastoma

#### **HEAD & NECK**

- Head & neck squamous cell carcinoma (HNSCC)
- Nasopharyngeal
- Thyroid

#### LIVER & BILIARY

- Biliary tract
- Hepatocellular carcinoma (HCC)

KIDNEY

- Renal cell carcinoma
- (RCC)

- **CHEST/THORACIC** 
  - Esophageal
- ↓ EGFRm non-small cell lung cancer (NSCLC)
- Image: Non-squamous NSCLC
- Quamous NSCLC
- Small cell lung cancer (SCLC)
  - Pleural mesothelioma

#### GASTROINTESTINAL

- Colorectal (all comers)
- Colorectal (MSI-H / dMMR)
- Gastric / Gastroesophageal junction (GEJ)
- Primary peritoneal

- Anti-VEGF approvals
- Anti-PD-(L)1 approvals
- Anti-VEGF and anti-PD(L)-1 approvals
- Ongoing / announced global study from Summit or **BioNTech**

#### **TISSUE-AGNOSTIC**

- High microsatellite instability (MSI-H) / deficient DNA mismatch repair (dMMR)
- High tumor mutational burden (TMB-H)

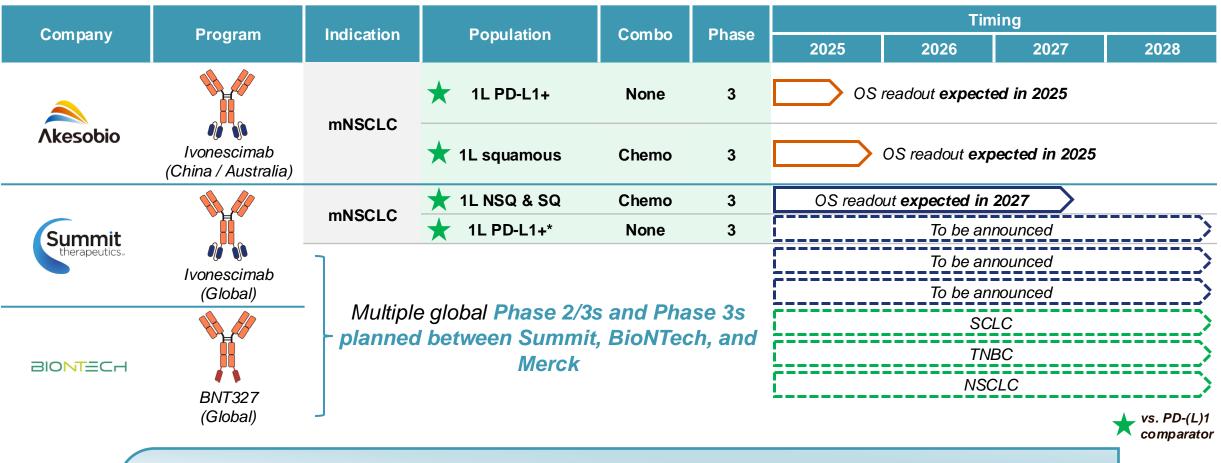
#### SKIN

- Basal cell carcinoma
- Cutaneous squamous cell carcinoma
- Melanoma
- Merkel cell carcinoma

Notes: EGFRm = mutant epidermal growth factor receptor.

Sources: Keytruda Label; Opdivo Label; Tecentrig Label; Imfinzi Label; Libtayo Label; Bavencio Label; Jemperli Label; Logtorzi Label; Zynyz Label; Avastin Label; Cyramza Label; Lenvima Label; Votrient Label

# Development programs across key late-stage competitors include numerous P3s with PFS & OS readouts, paving the way for CR-001



Multiple Phase 3s across leading PD-(L)1 x VEGF programs, with similar expected cooperativity to CR-001, should generate a multitude of PFS & OS catalysts for years to come



\*Summit has announced P3 in 1L PD-L1+ NSCLC, monotherapy vs. pembro, but has not released trial details. Notes: List of trials is not exhaustive. NSCLC = non-small cell lung cancer; TNBC = triple negative breast cancer; SCLC = small cell lung cancer; NSQ = non-squamous; SQ = squamous. PFS and OS readouts estimated based on PEP (primary endpoints) and completion dates listed on ClinicalTrials.gov. Sources: ClinicalTrials.gov; Company websites; Company presentations

# Parallel clinical development paths offer potential for both first-in-class and lower risk opportunities for CR-001

Focus on potential first-in-class opportunities with rapid path to market (i.e., efficient development strategy, anticipated likelihood of PFS and OS success)

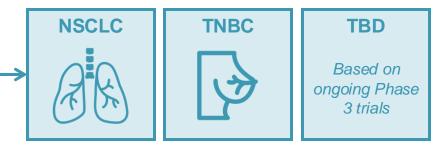
 Numerous indications with clinically meaningful anti-PD-(L)1 +/- VEGF efficacy and potential to combine with chemo / orthogonal MoAs.

Plan to rapidly follow ivonescimab in indications where clinical validation vs. anti-PD-(L)1 is highly differentiating

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High conviction that CR-001 can replicate ivonescimab's efficacy given similar construct & equivalent MoA.

#### POTENTIAL INDICATIONS





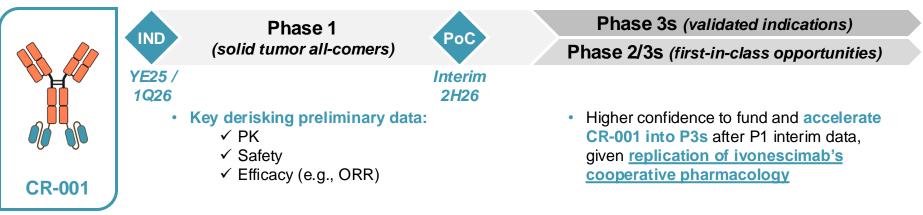
**CR-001** 

# CR-001 Phase 1 data offer potential for early de-risking – a rarity for a solid tumor oncology program

Phase 1 interim proof-of-concept data are a potentially significant value-generating event for CR-001.

- Preliminary data from early Phase 1 cohorts provides substantial validation of program because CR-001's structural design and preclinical data are similar to ivonescimab.
- Early Phase 1 data, as single agent and in combination with SoC, rapidly enables late-stage development in multiple solid tumor types, unlocking broad first-in-class and fast-follower opportunities.
- CR-001 is markedly differentiated from novel constructs disconnected from ivonescimab's MoA. Alternative formats may require significantly more patients' worth of safety and efficacy data in tumor-specific expansion cohorts and/or Phase 2s to establish conviction before initiating Phase 3s.

#### **ILLUSTRATIVE**



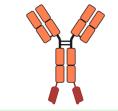
High conviction in CR-001's clinical profile can be reached in ~9-12 months from Phase 1 initiation, offering potential for significant early value inflection.



# Only <u>four</u> known constructs with potential to exhibit ivonescimab-like cooperative pharmacology

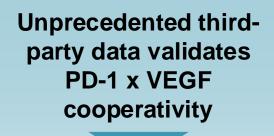






	Anti-PD-1 scFv-based		Anti-PD-1 VHH-based	Anti-PD- <u>L</u> 1 VHH-based
Program	CR-001	Ivonescimab	LM-299	BNT327 / PM8002
Company	CRESCENT	Summit therapeutics. Kesobio	MERCK     LaNova     A新医药	
Stage	Preclinical	Phase 3 (Global)	Phase 1/2 initiation (China)	Phase 2 (Global) / Phase 3 (China)
Anti-VEGF IgG	Bevacizumab	Bevacizumab	Bevacizumab	Bevacizumab
Anti-PD-(L)1	Anti-PD-1 scFvs	Penpulimab scFvs	Novel anti-PD-1 VHHs	Novel anti-PD- <u>L</u> 1 VHHs
Fc function	Fc null, to avoid potential AEs	Fc null, to avoid potential AEs	Fc null, to avoid potential AEs	Fc null, to avoid potential AEs
Cooperative pharmacology	$\checkmark$	$\checkmark$	Expected (not disclosed); unclear impact of VHH structure	Expected (not disclosed); unclear impact of PD-L1 VHH
<u>Examples</u> of alternative constructs	• Anti-PD-L1 IgG, with enhanced ADCC • VEGF trap	Anti-PD-1 mAb with off-target VEGFR2 binding through same variable domains	<ul> <li>Anti-PD-1 IgG</li> <li>Novel anti-VEGF VHHs</li> <li>Inverted format</li> </ul>	<ul> <li>Bevacizumab</li> <li>Anti-PD-1 Fabs</li> <li>PD-1 domains attached to IgG N- terminus instead of C-terminus</li> </ul>

## CR-001 preclinical data reproduces ivonescimab's breakthrough pharmacology and is rapidly advancing to generate significant value



Ivonescimab significantly **improved PFS versus pembrolizumab** in Phase 3 in 1L NSCLC – the first therapy to do so head-to-head

#### Transformative MoA for \$50B+ market

Poised to transform NSCLC standard of care, with broad application across \$50B+ anti-PD-(L)1 market CR-001's proprietary engineering is designed to replicate ivonescimab

CR-001 is a highly potent PD-1 x VEGF bsAb **reproducing cooperative binding** qualities critical to ivonescimab Built by the proven Paragon team

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Paragon has a demonstrated track record discovering and developing best-in-class molecules



### CR-002 & CR-003

Topoisomerase inhibitor ADCs against validated targets

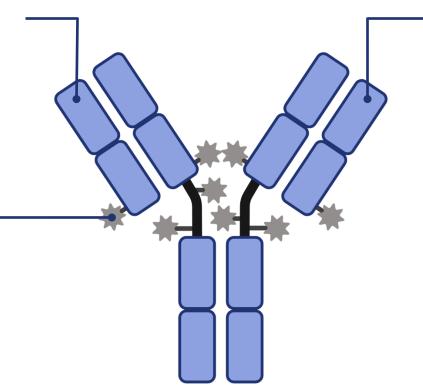
# CR-002 and CR-003 are potentially best-in-class topoisomerase inhibitor ADCs, with applicability across solid tumors

#### Validated, undisclosed solid tumor ADC targets

 Each unique target has potential in multiple solid tumor indications

### Best-in-modality topoisomerase inhibitor payloads

- Topoisomerase inhibitor payloads have consistently demonstrated superior efficacy and safety over microtubule inhibitor payloads
- Each ADC is expected to have
   bystander-killing effect



### Potential to synergize with CR-001 and other immunotherapies

- Each ADC can be leveraged in combination studies in solid tumors
- Multiple indications with ongoing PD-(L)1 x VEGF bispecific development and *separate* development of ADCs help de-risk clinical path for combinations

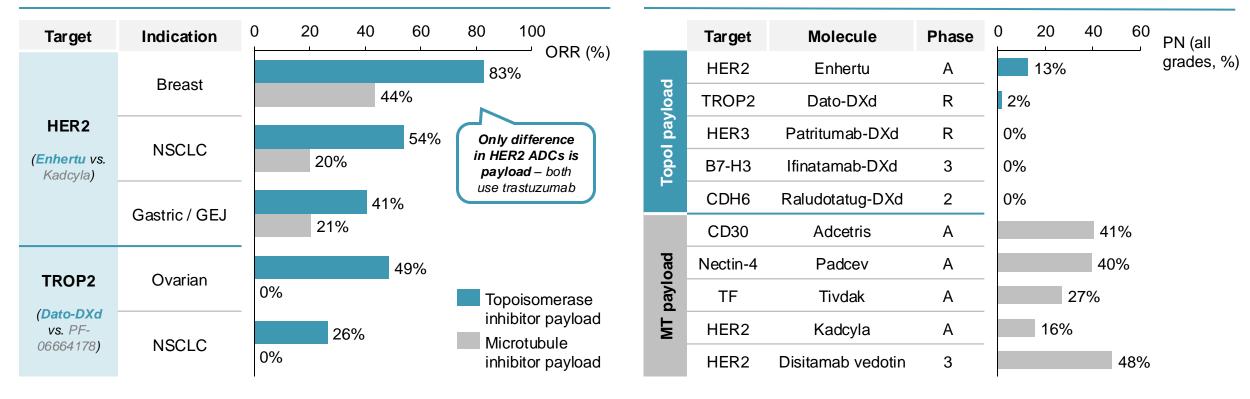
Targets for CR-002 and CR-003 to be disclosed as programs approach IND.



### ADCs with topoisomerase inhibitor payloads have demonstrated best-in-modality efficacy and safety CROSS-TRIAL COMPARISONS

Topol payload-based ADCs have **demonstrated superior ORR** vs. microtubule inhibitor-based ADCs in cross-trial comparisons...

... and have shown much lower rates of peripheral neuropathy, a critical AE that can drive dose reductions & discontinuations



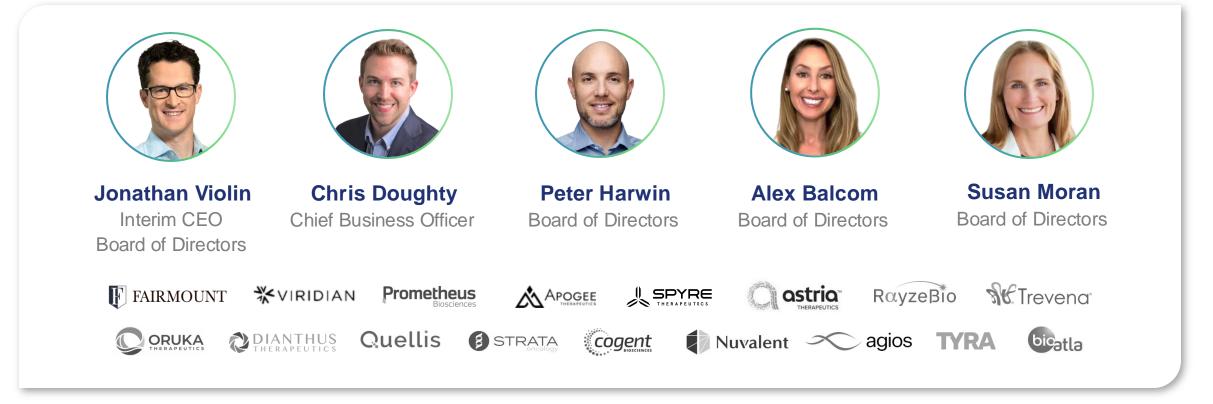
CR-002 and CR-003 utilize the best-in-ADC payload in their potentially best-in-class profiles.



Notes: NSCLC = non-small cell lung cancer; GEJ = gastroesophageal junction; A = approved; R = in registration. PN rates are weighted averages, by number of patients, across indications / trials and include PN, PSN, PMN, and PSMN when separately measured; full list of trials and references available on request. Disitamab vedotin is approved in China and in Phase 3 development globally. Sources: Enhertu Label; 2024 Smit (Lancet Onc); Kadcyla Label; 2019 Peters (Clin Cancer Res); 2017 Thuss-Patience (Lancet Onc); 2024 Oaknin (ESMO Pres); 2024 Ahn (JCO); 2018 King (Invest New Drugs)



## Rapidly growing leadership team with deep experience building the next generation of biotechnology companies



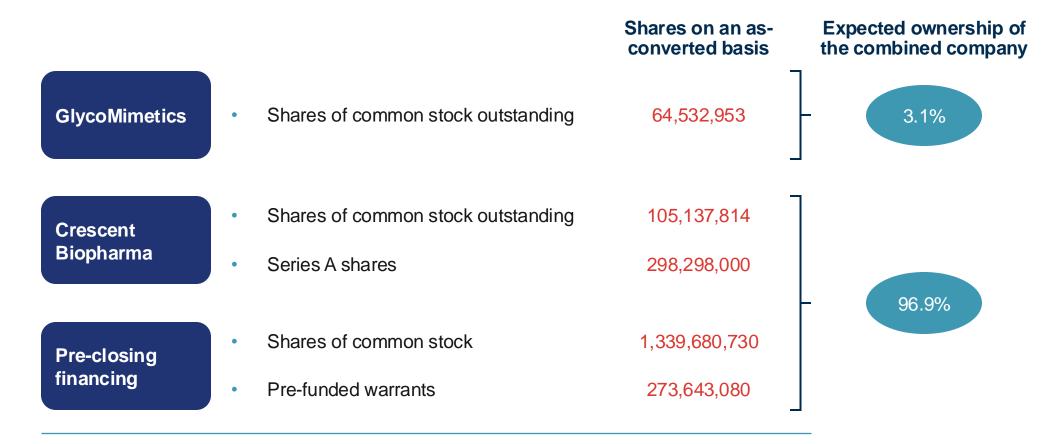


## Financing expected to fund Crescent programs through key anticipated value-generating catalysts

	2025	2026	
<b>CR-001</b> (cooperative PD-1 x VEGF bsAb)		YE25 / 1Q26: IND 2H: Initial clinical data	
<b>CR-002</b> (undisclosed, ADC #1 with Topol payload)	2H: DC	Mid-year: IND	
<b>CR-003</b> (undisclosed, ADC #2 with Topol payload)		1H: DC	
Key external events	1H: BNT327 P2/3 EGFRm NSQ mNSCLC interim ( 1H: Ivo P3 1L SQ mNSCLC interim (China) <b>2H: Ivo P3 HARMONi-2 1L mNSCLC OS (</b> 2H: BNT327 P2/3 1L ES-SCLC interim (China 2H: Ivo P3 HARMONi EGFRm NSQ mNSCLC interim 2H: Ivo P3 HARMONi-A EGFRm NSQ mNSCLC completed	(China) Multiple P3 trials ongoing or planned (e.g., SCLC, TNBC, NSCLC), with numerous PFS & OS readouts expected in 2026 and beyond	



### Estimated capitalization following close of transactions



### Estimated total shares of common stock of the combined company post-closing

2,081,292,577







