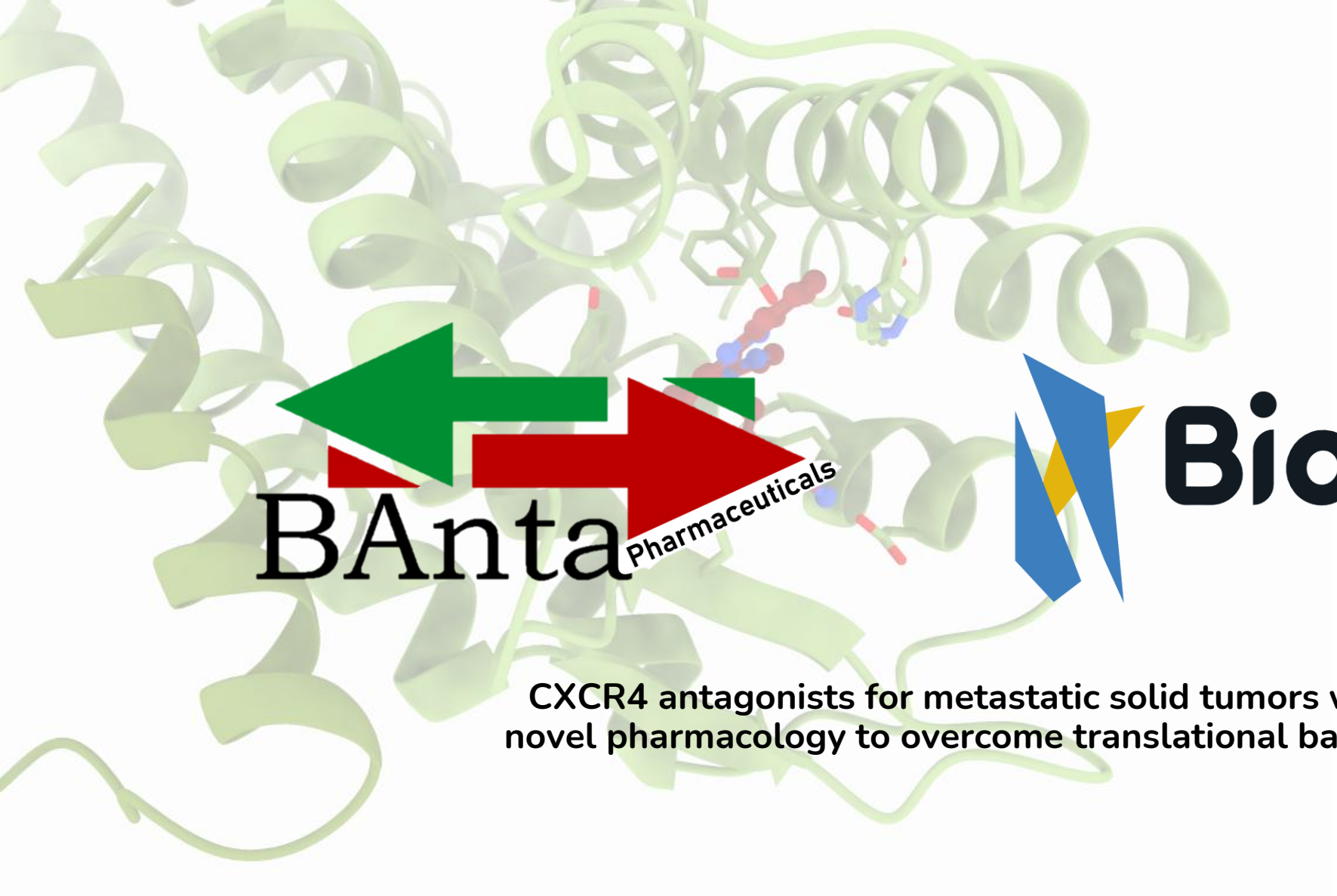

BAnta Pharmaceuticals

Biagon Inc.

CXCR4 antagonists for metastatic solid tumors with novel pharmacology to overcome translational barriers

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CXCR4 antagonists for solid tumors are a clinical graveyard

*CXCR4 is **highly expressed** in > 20 types of cancer*

*CXCR4 antagonists combined treatments consistently **fail** to meet efficacy endpoints for solid tumors*

***Loss of efficacy due to antagonist tolerance** may prevent adequate CXCR4 antagonist solid tumor treatments*

Sponsor	Asset	Indication	Phase I	Phase II	Phase II
Johns Hopkins Medicine	*Plexifor*	*Pancreatic Cancer*	●	🪦	
Stanford	*Plexifor*	*Glioblastomas*	●	🪦	
X4 Pharmaceuticals	*Mavorixafor*	*Renal Cancer*	●	🪦	
bioline rx	*Motixafortide*	*Pancreatic Cancer*	●	?	
Columbia University	*Motixafortide*	*Pancreatic Cancer*	●	?	
Lilly	*LY2510924*	*SCLC*	●	🪦	
Tcmbio	*PTX-9908*	*Hepatocellular Cancer*	●	?	
Bristol Myers Squibb	*Ulocuplamab*	*Solid Tumor*	●	🪦	
SPEXIS	*Ulocuplamab*	*HER2- Breast Cancer*	●	●	🪦

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CXCR4 β-arrestin-biased antagonist for solid tumors to overcome tolerance

Why CXCR4 for solid tumors?

- The CXCR4/CXCL12 signaling axis modulates tumor:
  - Proliferation
  - Survival
  - Angiogenesis
  - Migration
- Disruption leads to:

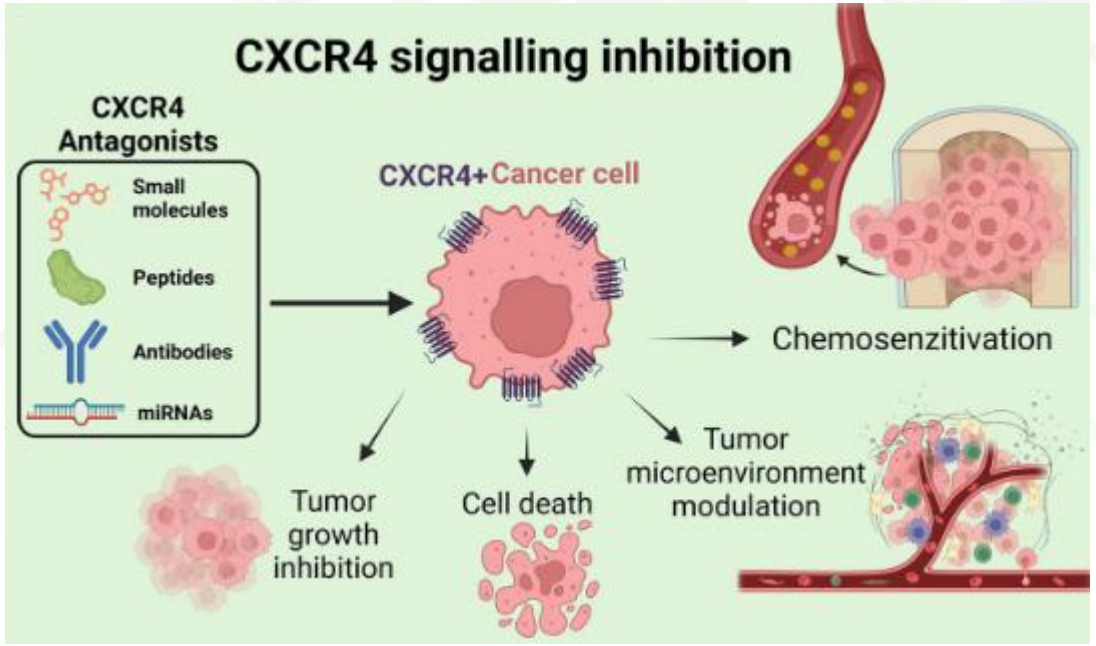

Figure adapted from Rueda, A. et al., (2025). Biomark.

Why a β-arrestin biased CXCR4 antagonist?

- Cell migration assays **become tolerant** to inhibition by Plerixafor (AMD3100) after 72 hours
- Cell migration assays ***do not*** **become tolerant** to a biased allosteric antagonist (X4-2-6) after 72 hours
- Tolerance is mediated by an **increase in CXCR4 cell surface expression**
- Increased expression results from inhibition of **β-arrestin-mediated endocytosis**

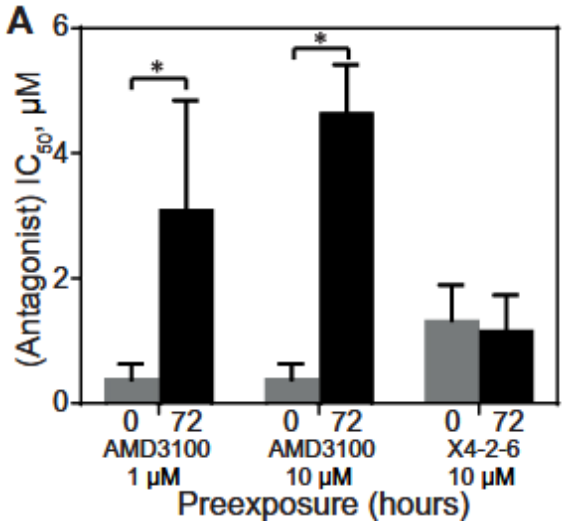

Figure adapted from Hitchinson, B. et al., (2018). Sci. Signal.

A β-arrestin biased antagonist of CXCR4 could ***preserve anti-tumor effects*** *of CXCR4 antagonists* ***without development of tolerance***

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Hitchinson, B. et al., (**2018**). *Sci. Signal.;* Rueda, A. et al., (**2025**). *Biomark*.

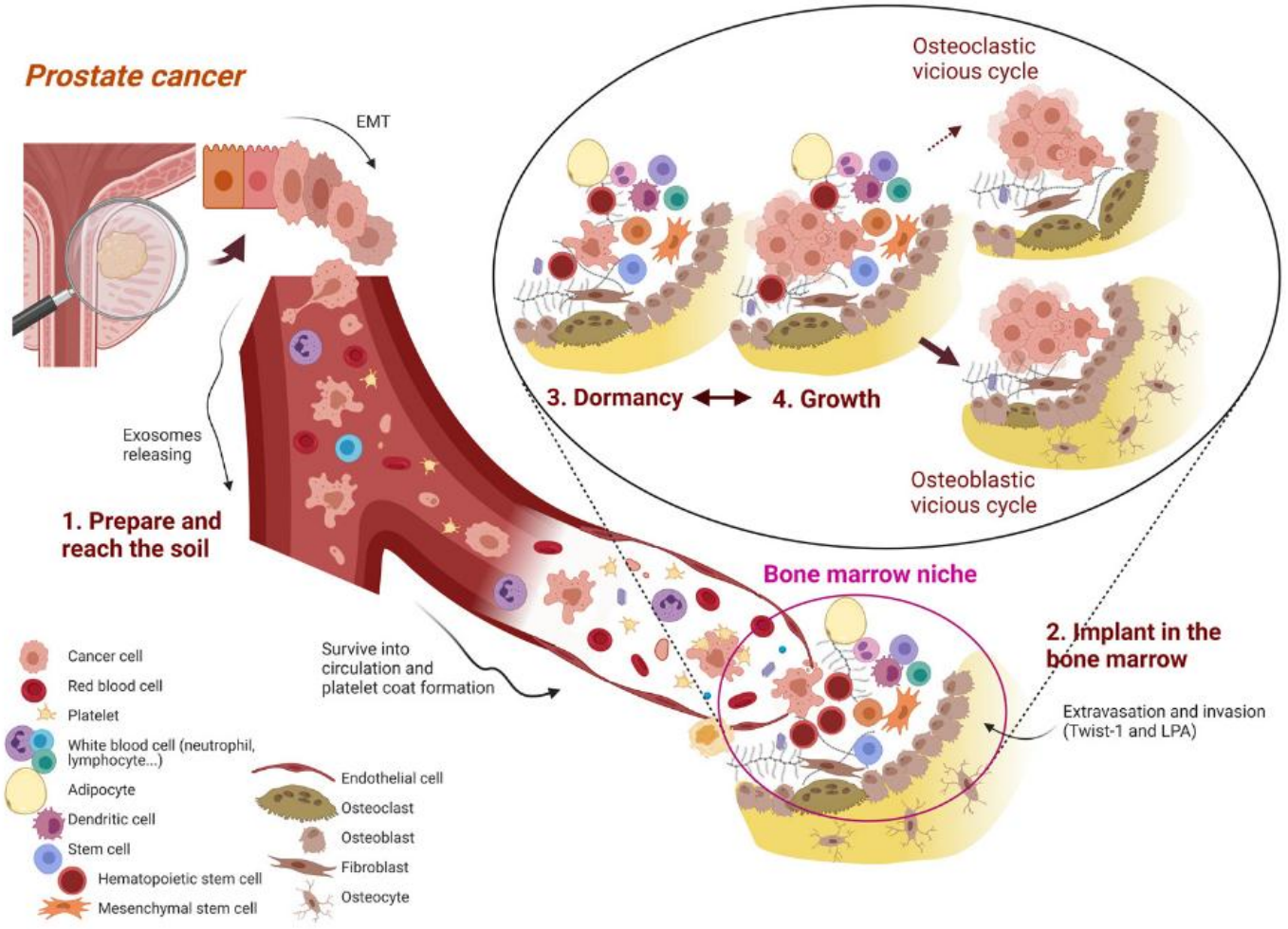
CXCR4 β-arrestin-biased antagonist for metastatic castration-resistant prostate cancer (mCRPC)

What role does the CXCR4/CXCL12 axis play in prostate cancer?

- CXCR4/CXCL12 signaling axis drives **bone marrow homing** mimicking stem cell homing
- CXCR4 expression is a **superior predictor of bone metastasis** v. the Gleason score
- Inhibiting CXCR4 with Plerixafor **decreased detectable bone lesions and overall survivability** in mice

How does inhibiting the CXCR4/CXCL12 axis answer patient unmet need?

- Inhibiting metastasis and bone marrow homing may improve:
  - Prognosis
  - **Distant metastases**
  - Recurrence
  - Overall survivability
  - **Skeletal-related events (SREs)**



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Akashi T. et al., (**2008**) *Jap. Canc. Assoc.*; Baldessari, C. et al, (**2023**). *Cancers*; Gravina, G. et al., (**2015**) *The Prostate*;

Collaboration to develop CXCR4 β-arrestin-biased antagonists

biased CXCR4 development candidates

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