

# Preclinical Research in the Age of FDA Modernization and AI

ONCOLOGY  
INTELLIGENCE



**CERTIS** | ONCOLOGY  
INTELLIGENCE®

- ✓ Headquartered and operated in San Diego, California, USA
- ✓ 10,000-mouse vivarium, precision-focused analytical capabilities
- ✓ CLIA certified for high-complexity testing
- ✓ AAALAC/IACUC accredited
- ✓ Expertise in solid tumors, orthotopic engraftment, and metastatic cancers (including intracranial)
- ✓ Patented predictive artificial intelligence platform supports more informed preclinical decision-making

# Optimizing Preclinical Models | Why and Why Now?

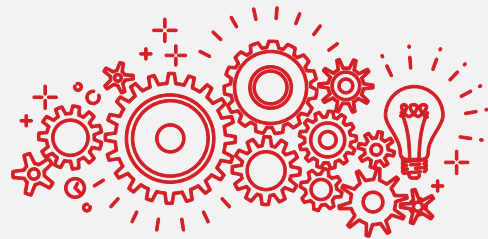
IT IS MORE IMPORTANT THAN EVER

1



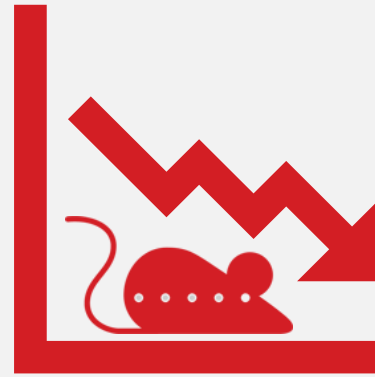
Persistent high failure rates in oncology drug development

2



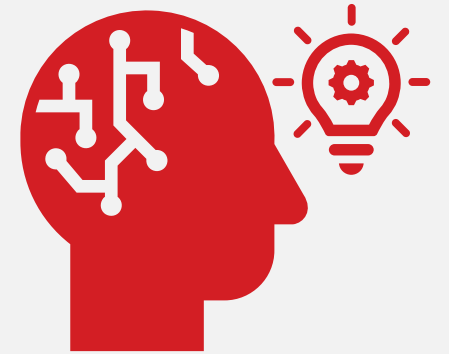
More complex therapies/targeting/mechanisms of actions

3



Desire to reduce number of animals used in drug research

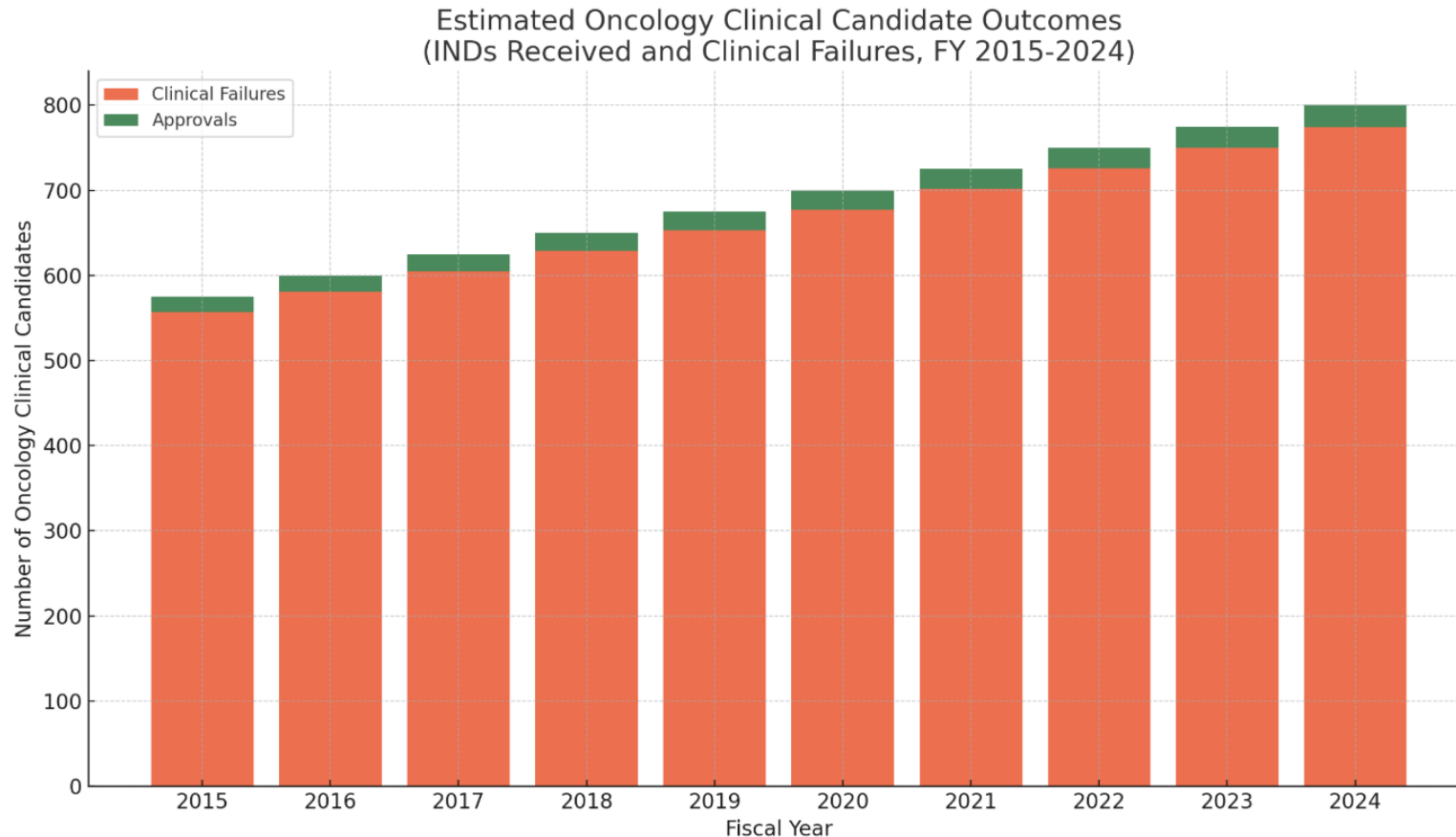
4



Opportunities presented by Artificial Intelligence

# Why and Why Now #1 | High Cost of Failure Limits Innovation

>95% OF PHASE 1 ONCOLOGY PROGRAMS RESULT IN CLINICAL FAILURE\*



>13,697\*\*  
CANCER DRUGS  
IN DISCOVERY/PRECLINICAL  
DEVELOPMENT

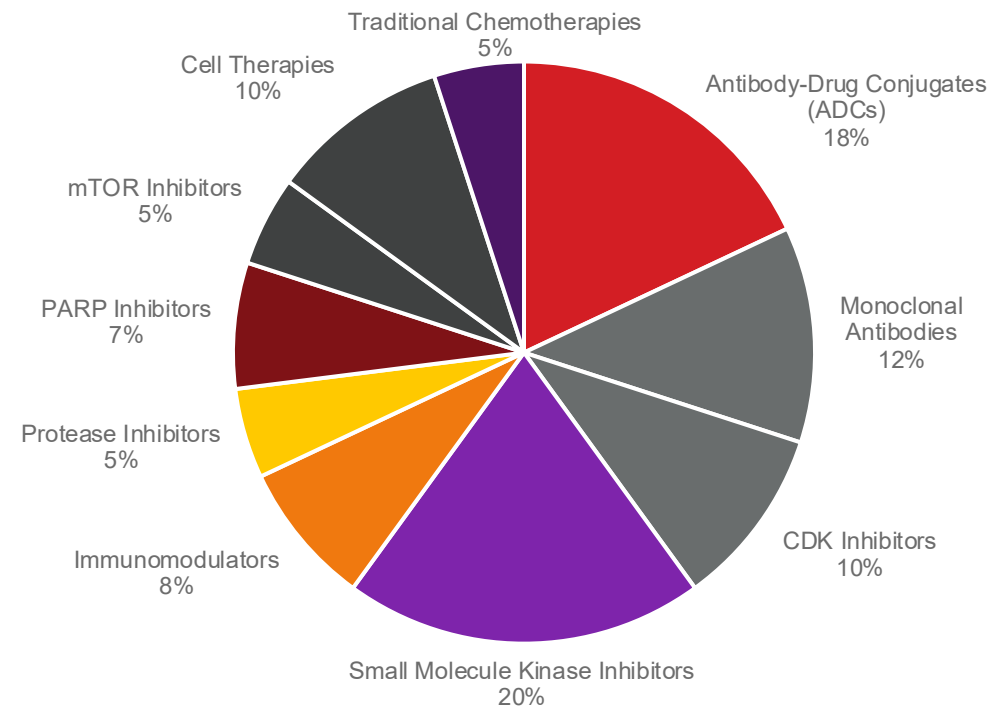
\*Biomedtracker, Citeline, February 2024

\*\*\*GlobalData 6/10/25

# Why and Why Now #2 | More Complex Therapies

## ADCS, IMMUNOTHERAPIES, BISPECIFIC ANTIBODIES AND MORE

- Complex MoA
- Tumor Heterogeneity
- Target Validation in Clinically Relevant Contexts
- Predicting Resistance and Toxicity
  - Resistance mechanisms
  - On-target, off-tumor toxicity
- Translatability



Preclinical Oncology Pipeline by Molecule Type

# Why and Why Now #3 | Evolving Regulatory Context

## PROXY SYSTEMS HAVE THEIR PLACE, BUT ALSO SIGNIFICANT LIMITATIONS

Organoids and organ-on-chip systems



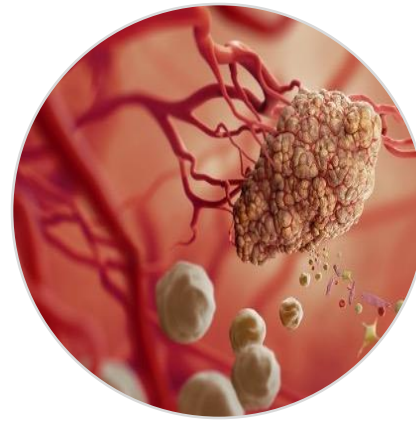
- Lack of systematic physiology
- Limited immune system integration
- Inability to assess metastasis in vivo

In vitro assays using human cells



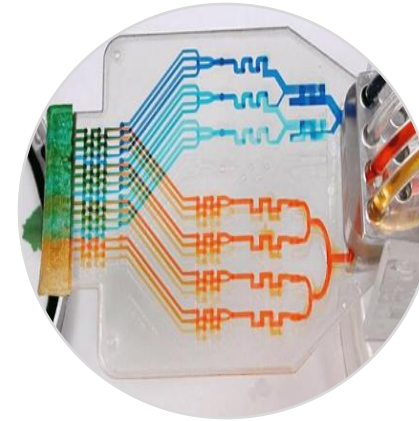
- No tumor microenvironment
- No immune system context
- Unable to study in vivo tumor progression

3D Tumor Microenvironments



- No vasculature or real perfusion
- Limited immune-tumor interaction
- Absence of systematic drug effects and toxicity in multiple organs and off-target tissue

Microfluidic Platforms



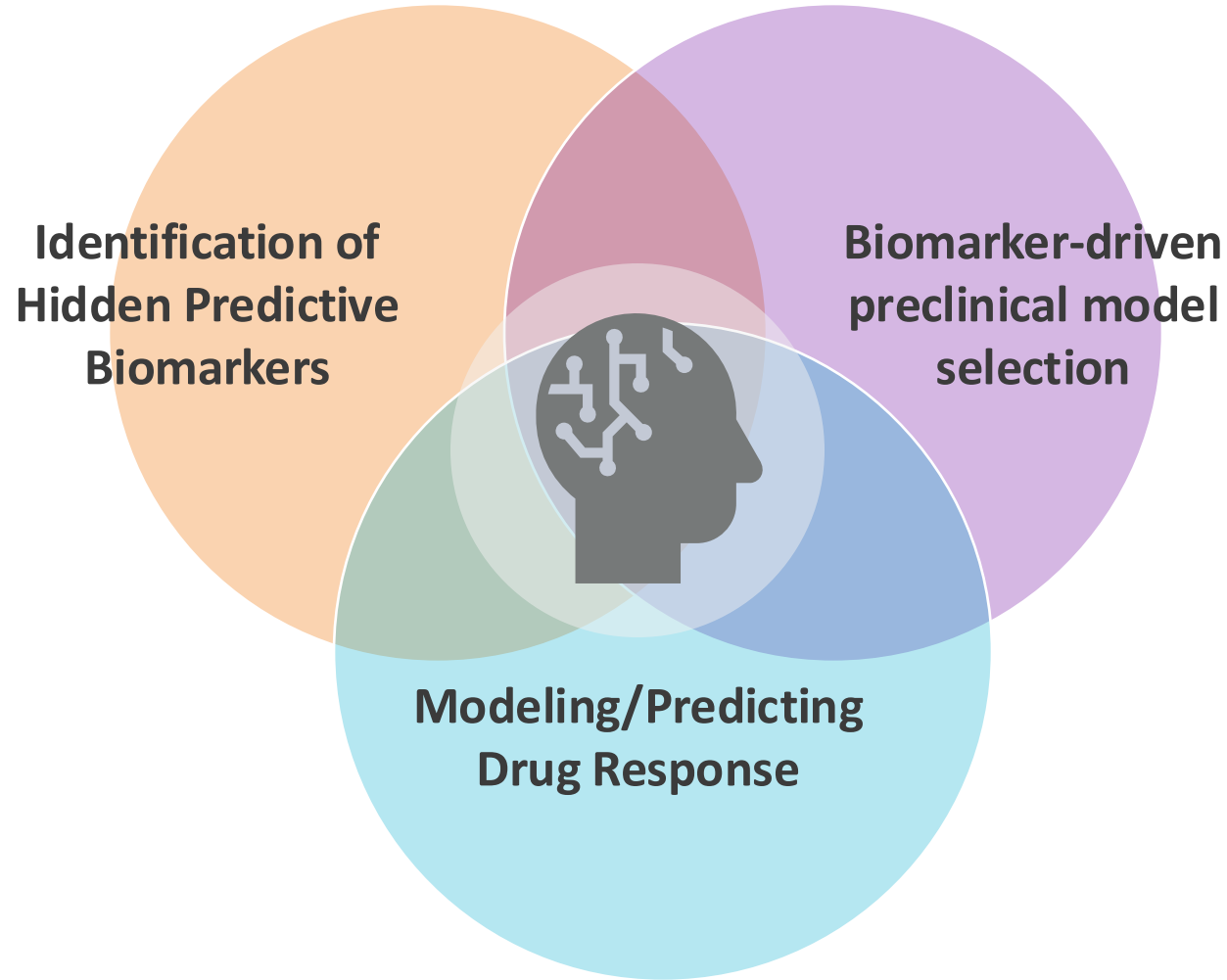
- Restricted to localized modeling
- Limited immune surveillance
- Lack of pharmacokinetic surveillance

Computational & AI Simulations



- Inability to simulate cancer's physiological complexity
- May not capture off-target effects or toxicity in real tissues

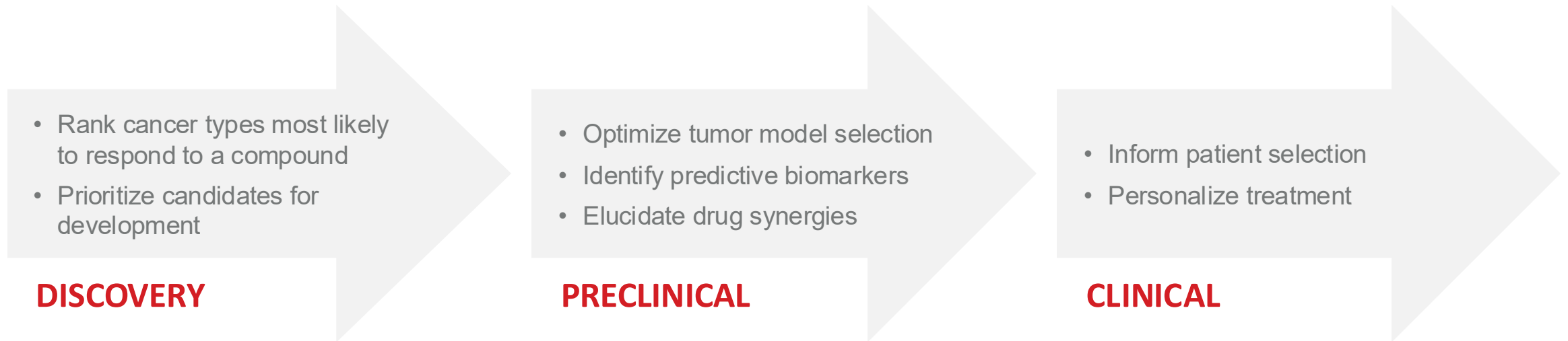
# Why and Why Now #4 | Integration of Artificial Intelligence



Computational algorithms and *in silico* modeling enables deep evaluation of relationship between gene expression and drug response

# AI/ML in Drug Development | From Discovery to the Clinic

## AI-ENABLED INSIGHTS BRING PRECISION TO DECISION-MAKING



**CERTISAI™**  
PREDICTIVE ONCOLOGY INTELLIGENCE

# AI/ML In Drug Development | Selecting Optimal Models



- First chatbot digital assistant designed exclusively for cancer research
- Easy-to-use; built on ChatGPT natural language backbone
- Leverages power of CertisAI™ to perform complex ad hoc analyses
- Rapid visualization of results for instant insights

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**BARNEYOI CANCER MODEL DATABASE®**  
**COMPOSITION & FEATURED COLLECTIONS**

**CERTIS™**

# BarneyOI® | A Diverse Collection of PDX Tumor Models

650

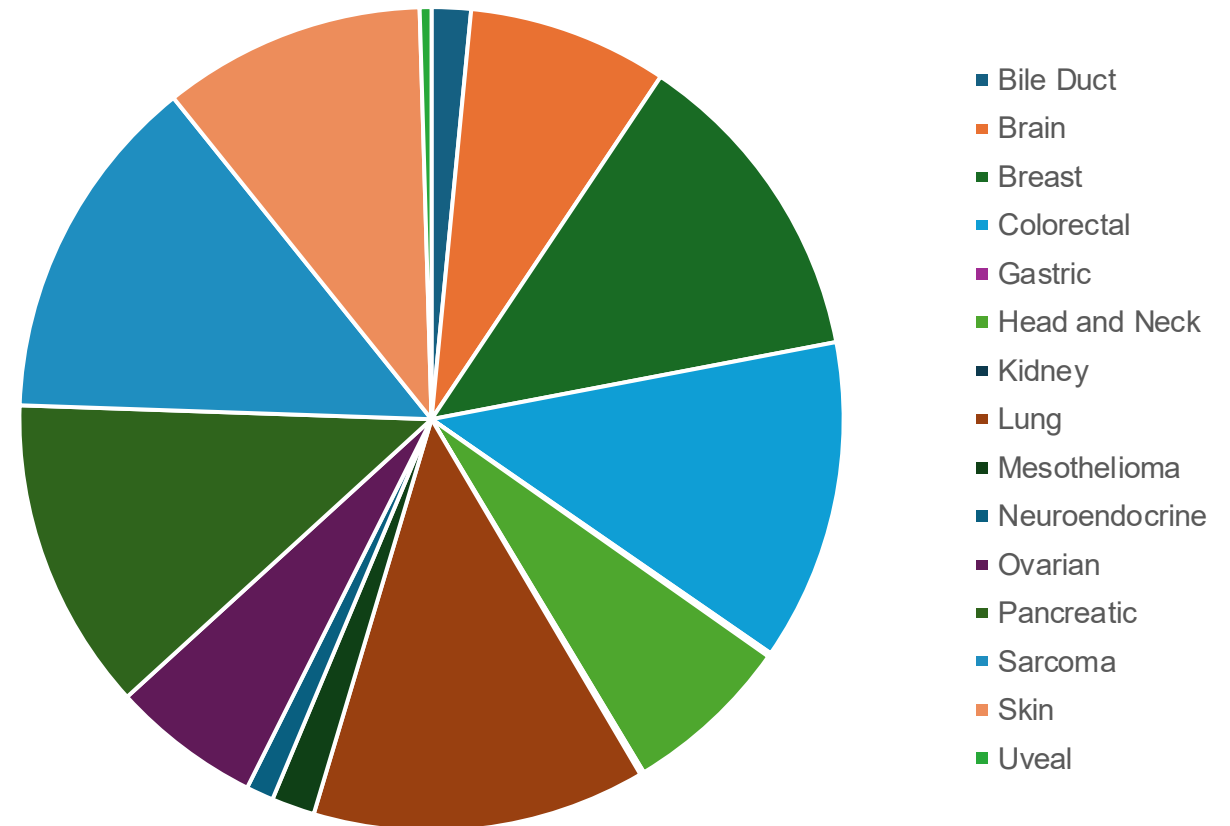
HIGHLY CHARACTERIZED & RICHLY ANNOTATED TUMOR MODELS

- Clinical History
- RNA Seq
- WES
- Fusion
- Deletion
- Amplification
- Histology
- Growth Kinetics
- Pharmacology
- MRI Images

BARNEYOI®

*Tumor bank composition as of 6/30/25. Includes PDX models and PDX-derived cell cultures/spheroids and patient-derived cultures*

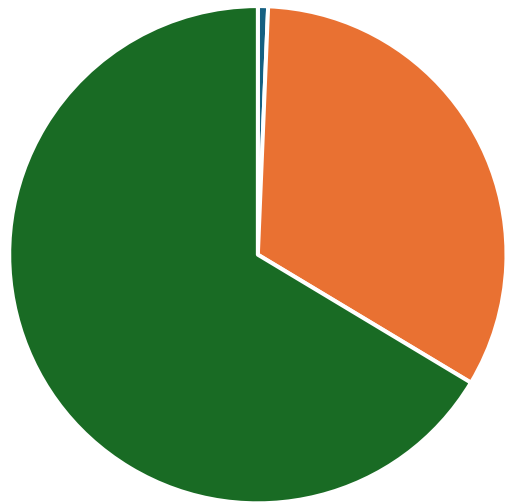
CERTIS PRECLINICAL CANCER MODELS BY CANCER TYPE



# BarneyOI® | A Diverse Collection of PDX Tumor Models

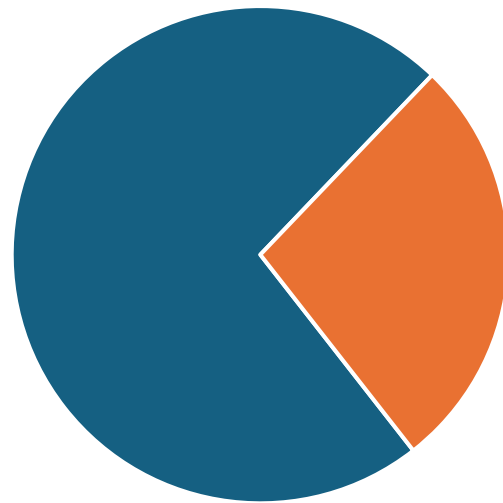
## BROAD REPRESENTATION ACROSS MANY FEATURES

Metastatic Status



■ Local Recurrence ■ Metastasis ■ Primary

Prior Treatment Status



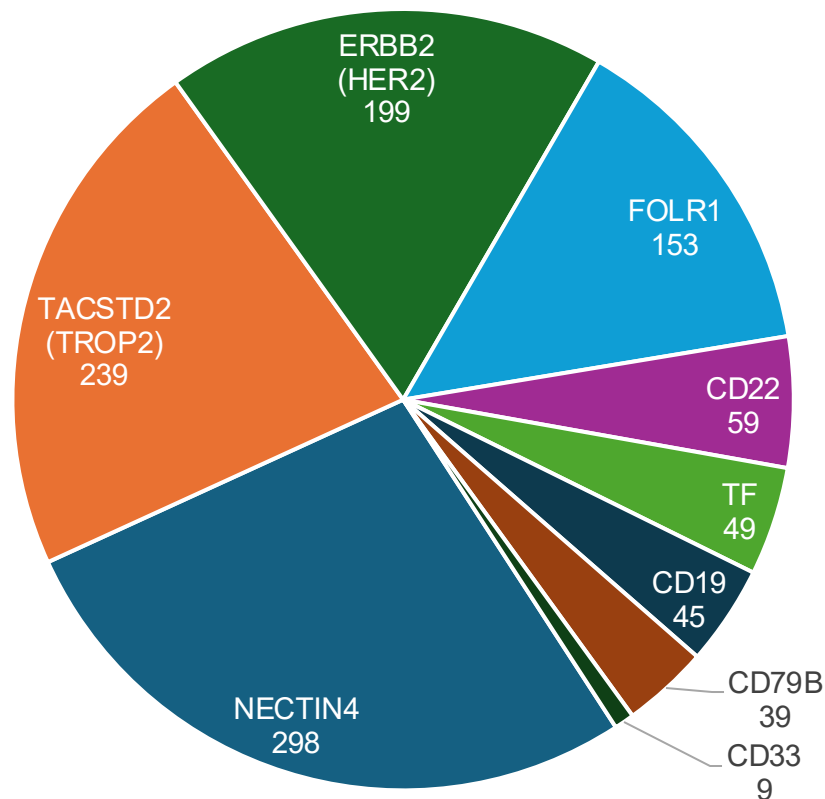
■ Chemotherapy ■ Targeted

Targeted Therapy Pretreatment Profile

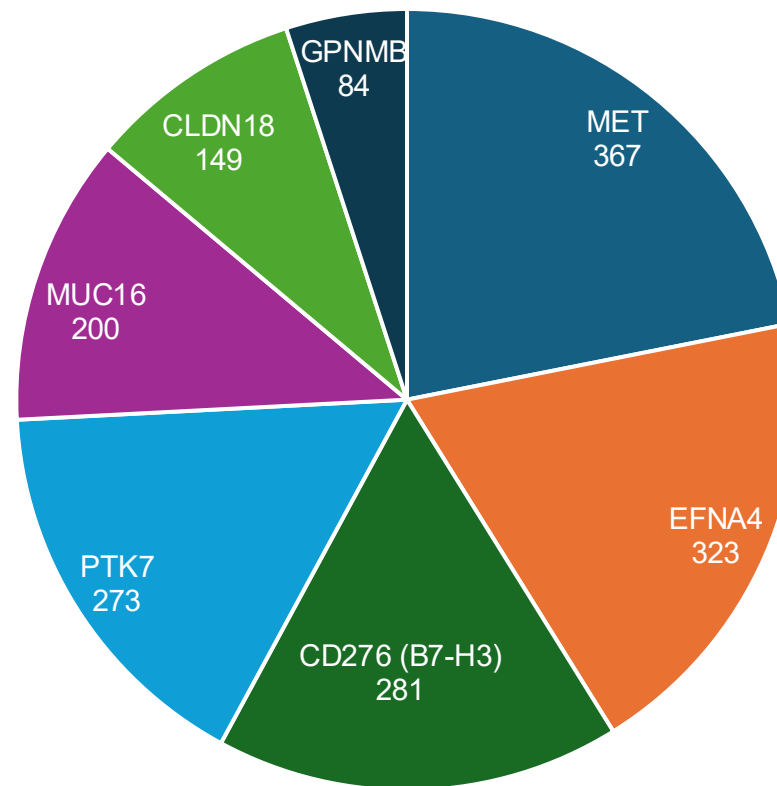


# BarneyOI® | A Diverse Collection of PDX Tumor Models

## COMMON ADC TARGETS

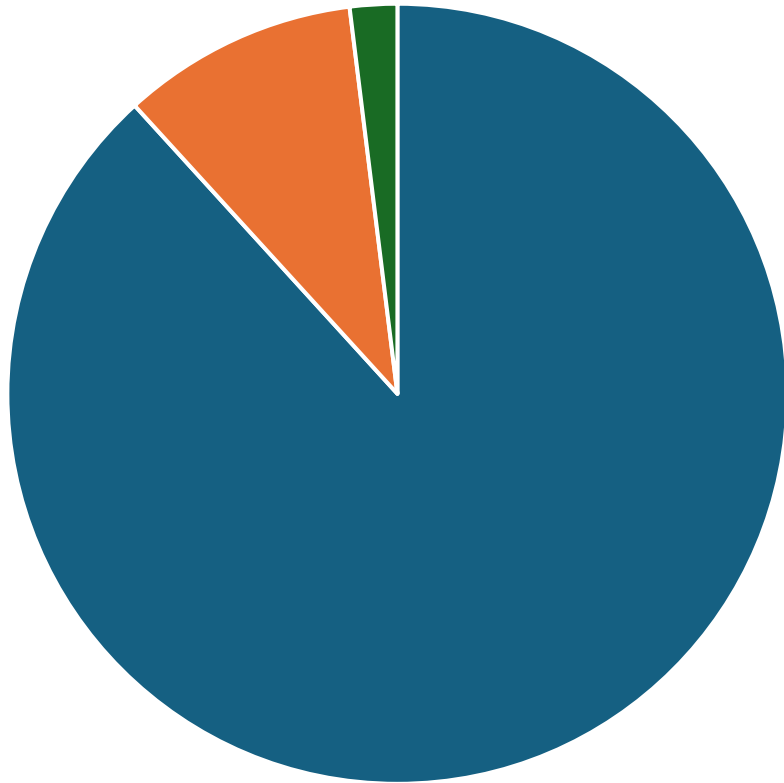


## NOVEL/EMERGING ADC TARGETS



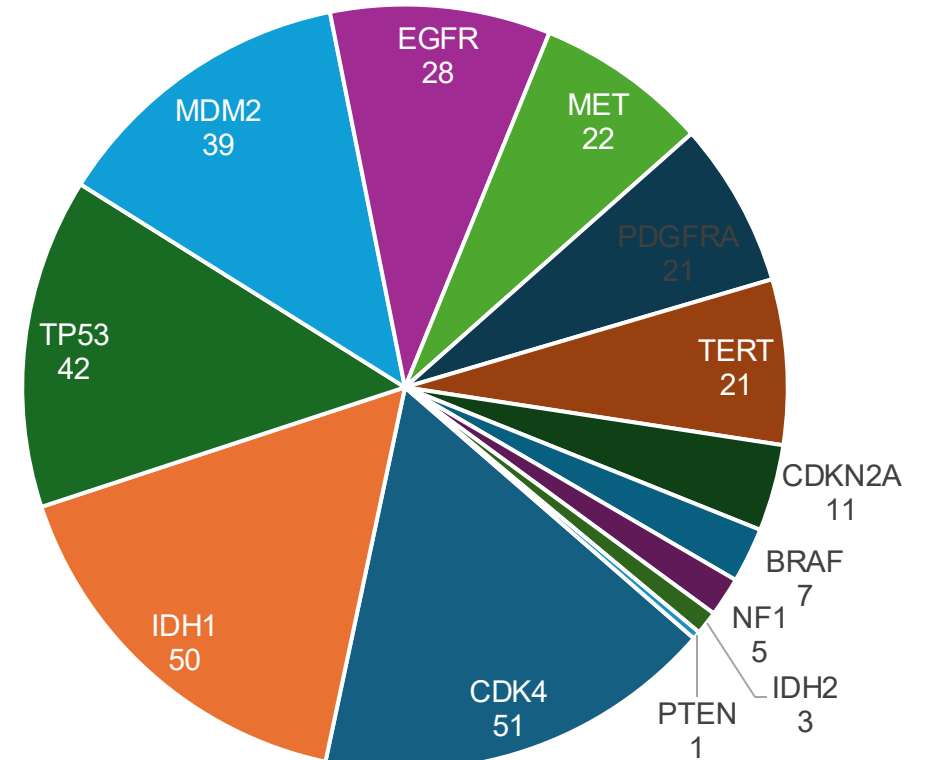
# Featured Collections | Brain Cancer Models

## 56 PDX, PDX-DERIVED & PATIENT-DERIVED MODELS



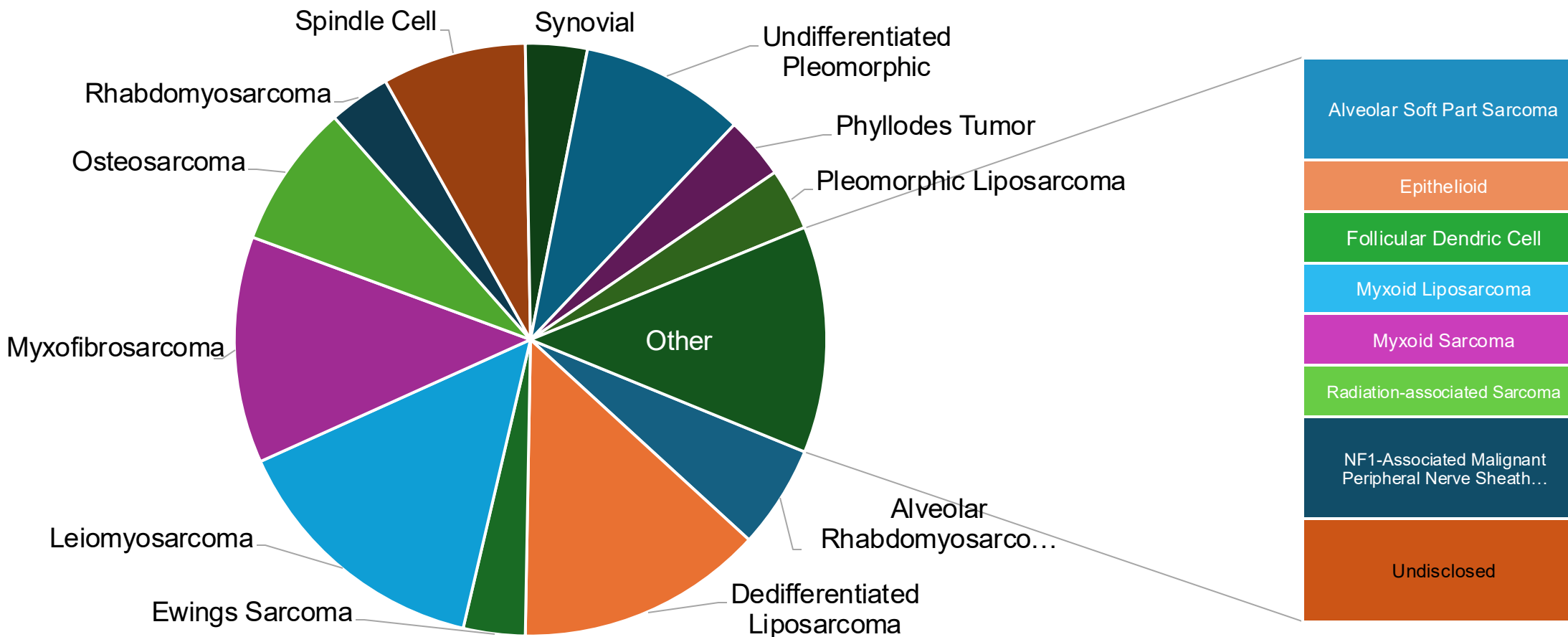
■ Glioblastoma ■ Gliosarcoma ■ Meningioma

## MODELS EXPRESSING COMMON GBM TARGETS



# Featured Collections | Sarcoma Models

## A COLLECTION OF 89 MODELS AS DIVERSE AS SARCOMA ITSELF



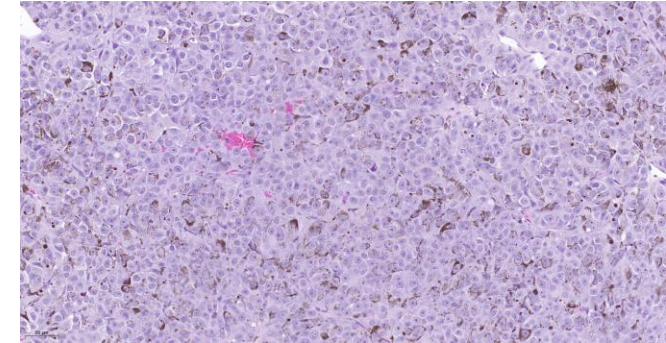
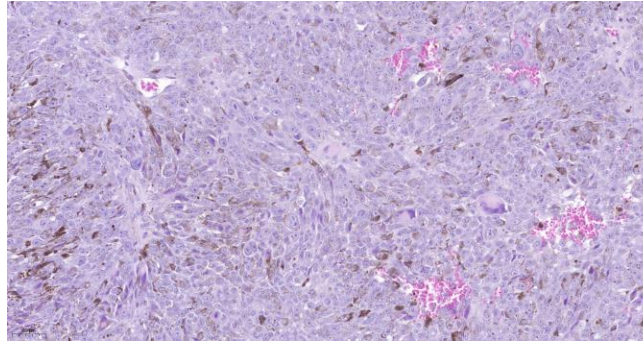
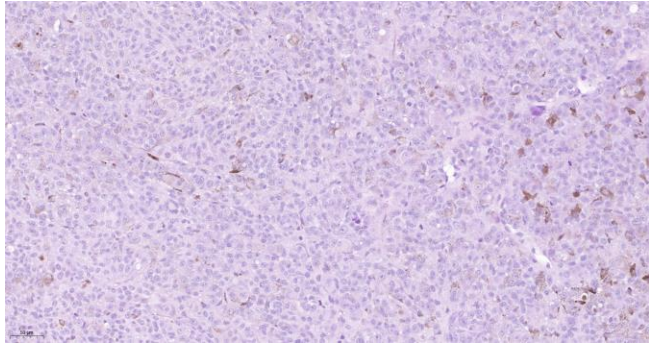
# Featured Collections | Uveal Melanoma Models

**CRT00819**

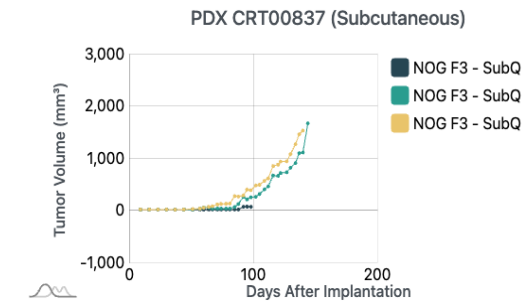
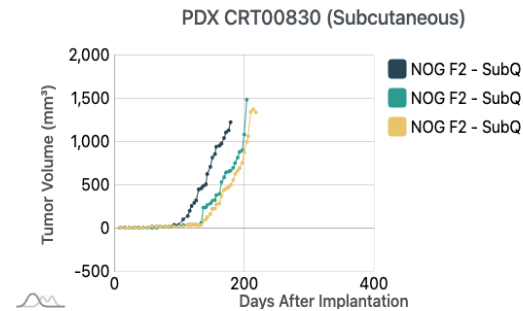
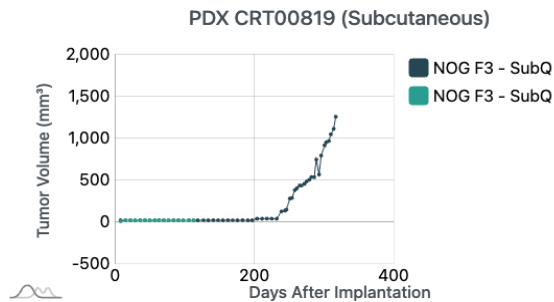
**CRT00830**

**CRT00837**

IHC



Growth Curve



Notable model details:

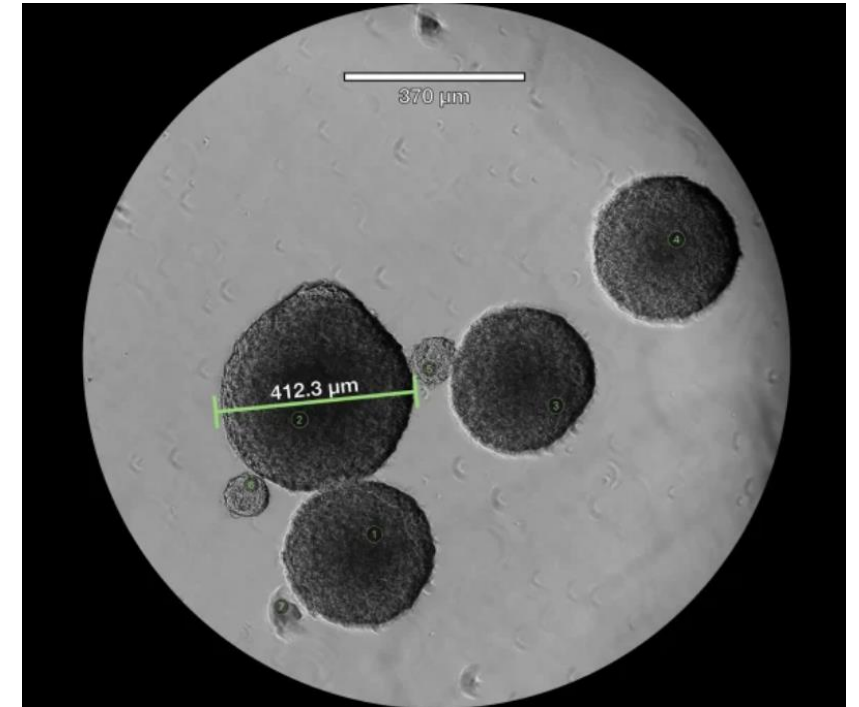
- All metastatic uveal melanoma PDX models from female patients
- All have received radiotherapy
- Tumor mutational burden and microsatellite instability are low-to-moderate

# Featured Collections | In Vitro/In Vivo “Matched Pairs”

## BRIDGE GAP BETWEEN CELL-BASED ASSAYS AND ANIMAL STUDIES

**51 models with matched PDX and PDX-cell culture pairs:**  
sarcoma | skin | breast | brain | lung | colorectal | neuroendocrine  
pancreatic | head and neck

- **Translational Relevance:** Aligns *in vitro* and *in vivo* drug responses.
- **Mechanistic Insight:** Validate *in vitro* pathway analyses *in vivo*.
- **Reduced Variability:** Increases confidence in observed differences.
- **Streamlined Drug Screening:** Enables confirmation of *in vitro* hits *in vivo*.
- **Biomarker Discovery:** Allows cross-system confirmation of predictive markers.
- **Resistance Modeling:** Study acquired resistance mechanisms *in vitro*, which can then be tested for clinical relevance *in vivo*.



Glioblastoma spheroids derived from our PDX models provide a paired platform for a seamless transition from *in vitro* to *in vivo* studies.

# BarneyOI Cancer Model Database®

**BARNEYOI**®  
CANCER MODEL DATABASE

**Request Access**

[info.certisoncology.com/request-access-to-barneyoi](https://info.certisoncology.com/request-access-to-barneyoi)



**BARNEYOI** Search

**CRT00316.001**  
Active Related Models

**Tumor Information**

Model Type: **PDX**

Biopsy Site: **Right foot**

HLA Status: **A24/A31, B27/B27, C17/C17**

TMA Number: **1**

Cancer Type: **Sarcoma**

Primary / Metastasis: **Metastasis**

Tumor Mutation Burden: **5.39**

Cancer Subtype: **Rhabdomyosarcoma**

Diagnosis: **Undisclosed**

Microsatellite Instability: **3.6**

**Patient Information**

Biological Sex: **F**      Age: **14**      Ethnicity: **Undisclosed**

Prior Treatment: **Treatment Naive**

**BARNEYOI** Assets

Search...

open all close all

**Model Summary** Gene Expression Gene Mutation Gene Fusion Copy Number Variation

Filter...

Model Id	Cancer Type	Cancer Subtype	Model Type	Patient Age	MSI	Tumor Mutation Burden
CRT00409.001	Pancreatic Cancer	Adenocarcinoma	PDX	64	3.97	0.74
CRT00311.001	Skin Cancer	Melanoma	PDX	68	3.61	6.83
CRT00444.002	Sarcoma	Aveolar Soft Part Sarcoma	PDX-derived cell culture		1.82	1.93
CRT00358.001	Brain Cancer	Glioblastoma	PDX	57	6.19	2.04
CRT00288.001	Sarcoma	Undifferentiated Pleomorphic Sarcoma	PDX	39	3.52	2.86
CRT00350.001	Sarcoma	Myxofibrosarcoma	PDX	76	3.12	0.57
CRT00502.001	Ovarian Cancer		PDX			1.44
CRT00449.001	Pancreatic Cancer	Pancreatic Adenocarcinoma	PDX	62		1.43
CRT00257.001	Sarcoma	Ewings Sarcoma	PDX	63		0.53
CRT00318.001	Sarcoma	Leiomyosarcoma	PDX	46	3.23	1.52
CRT00373.001	Pancreatic Cancer		PDX		3.56	2.28
CRT00077.001	Sarcoma	Undifferentiated Pleomorphic Sarcoma	PDX	67		
CRT00407.001	Ovarian Cancer	Ovarian Carcinosarcoma	PDX	42		
CRT00359.001	Brain Cancer	Glioblastoma	PDX	54	4.86	1.64
CRT00395.002	Sarcoma	Liposarcoma	PDX-derived cell culture		2.62	0.43

SEARCH | FILTER | VIEW | COMPARE | EXPORT

# MURINE PRECLINICAL MODELS

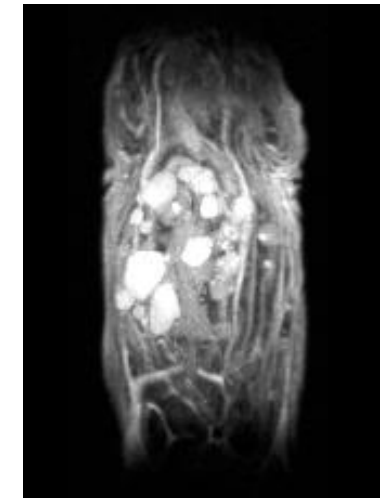
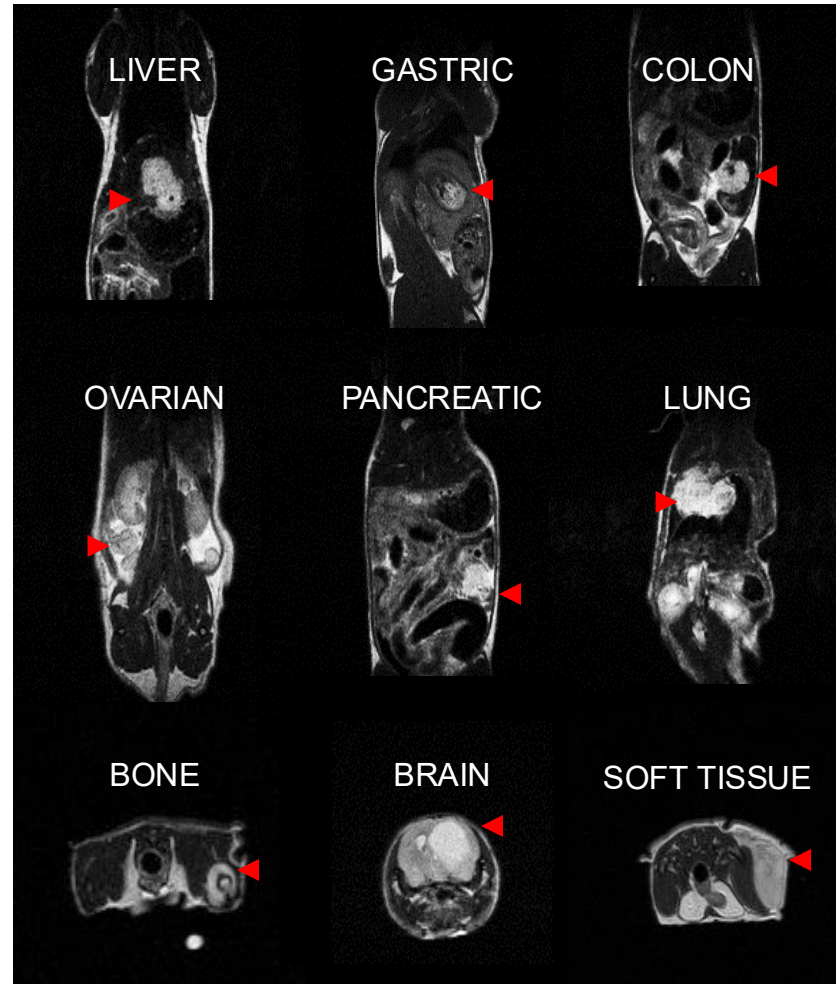
## NOT ALL ARE CREATED EQUALLY

- ✓ Engraftment Techniques
- ✓ Murine Strains
- ✓ Modeling Immune Response

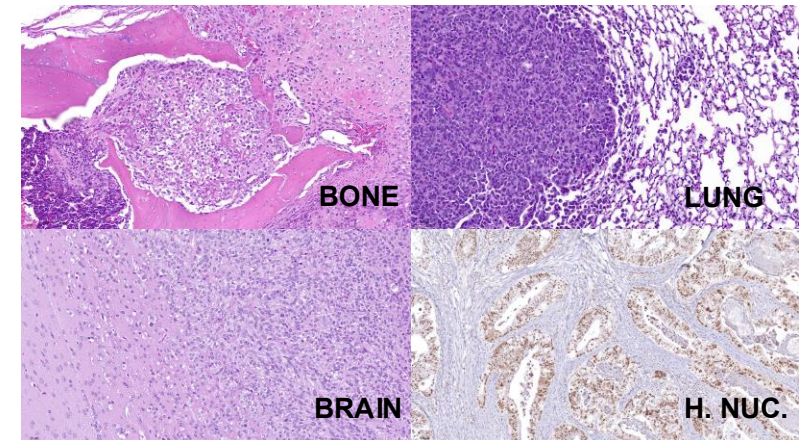
# SubQ vs. Orthotopic PDX | Clinical Relevance

## O-PDX: High Concordance with Human Condition

- ✓ Maintain histological characteristics of patient tissue
- ✓ Recapitulate tumor microenvironment
- ✓ Have propensity to metastasize
- ✓ Facilitate study of intracranial cancers
- ✓ Especially important for I-O therapies and solid tumors



3D MRI enables interrogation from multiple angles.



# Intracranial | Brain Cancer Studies

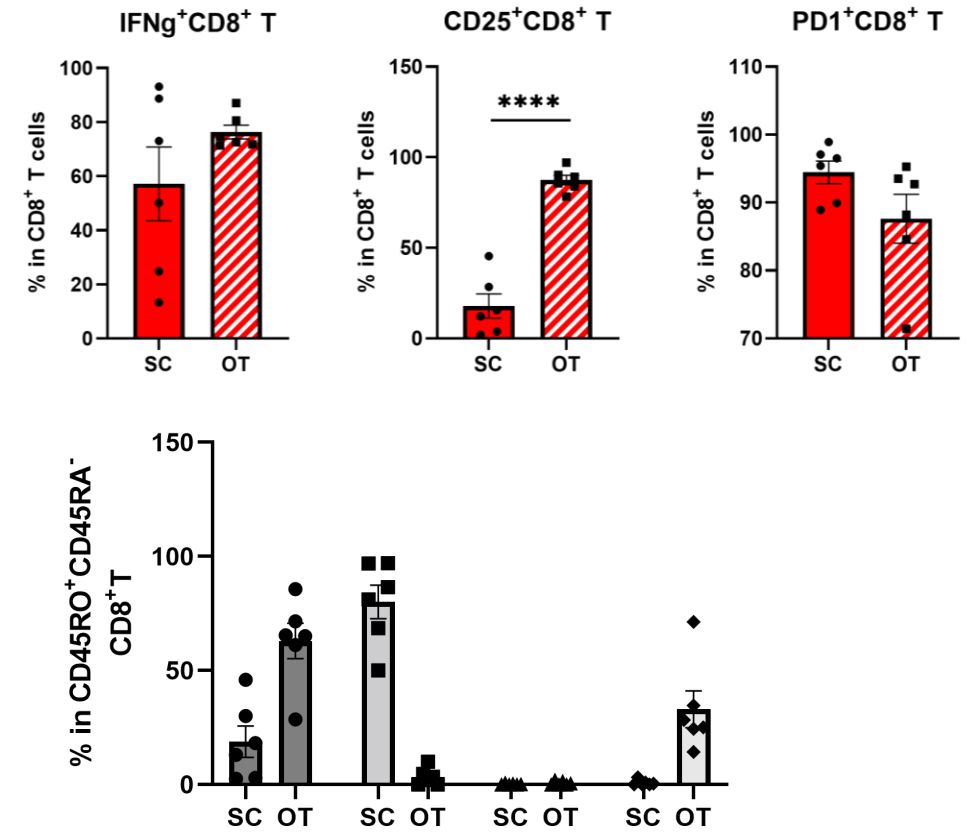
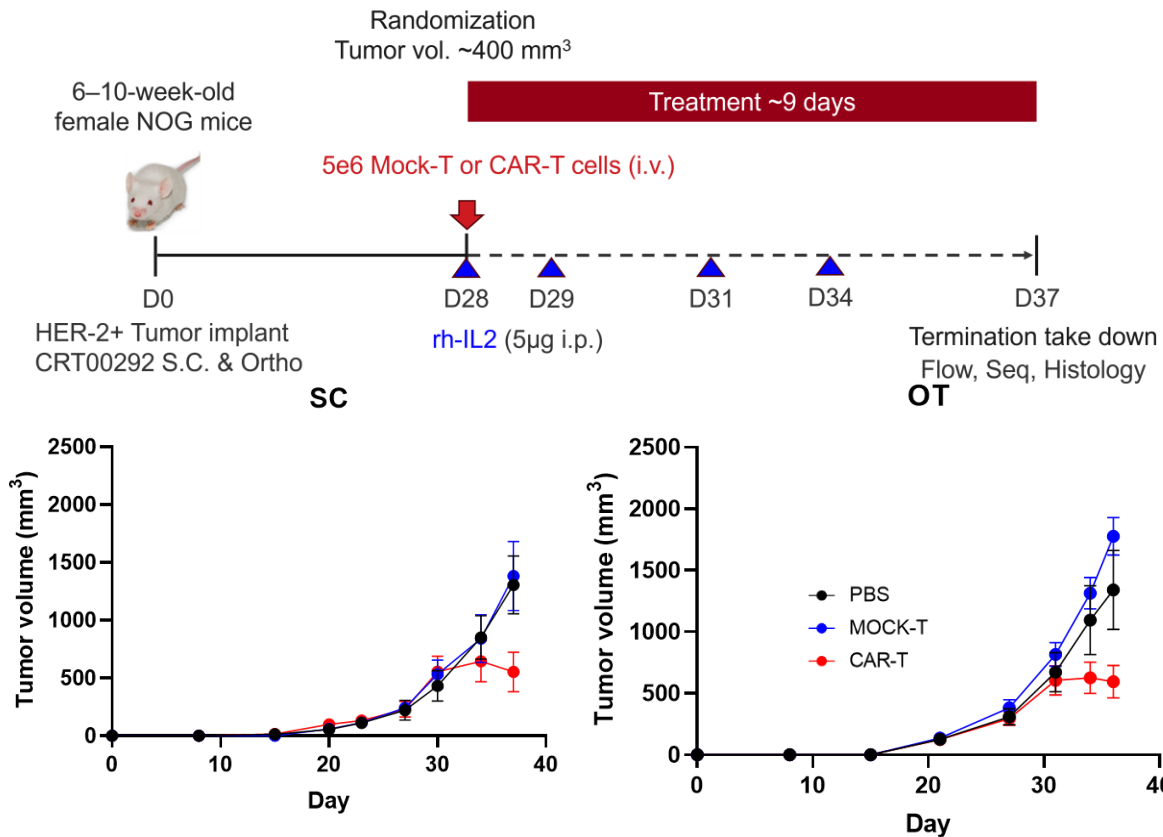
## STEREOTACTIC ENGRAFTMENT IN ORTHOTOPIC PDX MODELS


- Precise intracranial placement mimics native tumor site
- Replicates brain-specific microenvironment and tissue context
- Enables tumor-vasculature and stroma interaction studies
- More predictive than subcutaneous models
- MRI-compatible for *in vivo* monitoring



# HuPDX Models | Orthotopic vs. SubQ

## SIMILAR EFFICACY, BUT LESS TUMOR INFILTRATION AND TCM CELLS





We are an AI-enabled precision oncology and translational science company. Our product is “Oncology Intelligence”—highly predictive therapeutic response data derived from advanced models of cancer.

# The Certis Way | Our Corporate Culture

- **THE CERTIS WAY**

Innovation, collaboration, and the relentless pursuit of precision.

# Translational Services | Delivering Oncology Intelligence

## CERTISAI™

- Select optimal cancer models for *in vitro* and *in vivo* validation
- Identify predictive biomarkers
- Uncover biological pathway MOA
- Rank cancer types most likely to respond to candidate
- Elucidate synergistic potential of combinatory therapies
- Develop stratification strategies for patient selection
- Prioritize compound libraries
- Assess value of intellectual property

## CUSTOM MODELS

- Orthotopic PDX
- Subcutaneous PDX
- Humanized (PBMC/CD34/TILs)
- CDX cell lines
- Metastatic
- Resistant
- Radiation (precision and whole body)
- PDX-derived 3D spheroids



## IN VIVO

- Efficacy
- Tolerability
- PK/PD
- Co-clinical trials

## IN VITRO/EX VIVO

- 3D cell cultures
- Catalog cell lines
- Client-supplied cell lines



## ADVANCED IMAGING

- Murine-scale MRI
- Bioluminescence
- Fluorescence
- IncuCyte® Live Cell Imaging

## ENDPOINTS

- Spectral flow cytometry
- MSD®
- HTRF
- ELISA
- Immunoassays
- cfDNA
- Comprehensive IHC in-house

**CERTAINTY IS PRICELESS.  
HOW CAN WE HELP?**

[busdev@certisoncology.com](mailto:busdev@certisoncology.com)

# Citations

- (1) Gu A, Li J, Li MY, Liu Y. Patient-derived xenograft model in cancer: establishment and applications. *MedComm* (2020). 2025 Jan 19;6(2):e70059. doi: 10.1002/mco2.70059. PMID: 39830019; PMCID: PMC11742426.
- (2) Taglieri M, Di Gregorio L, Matis S, Uras CRM, Ardy M, Casati S, Marchese M, Poggi A, Raffaghello L, Benelli R. Colorectal Organoids: Models, Imaging, Omics, Therapy, Immunology, and Ethics. *Cells*. 2025 Mar 19;14(6):457. doi: 10.3390/cells14060457. PMID: 40136707; PMCID: PMC11941511.
- (3) Abdolahi, S., Ghazvinian, Z., Muhammadnejad, S. *et al.* Patient-derived xenograft (PDX) models, applications and challenges in cancer research. *J Transl Med* **20**, 206 (2022). <https://doi.org/10.1186/s12967-022-03405-8>
- (4) Chen C, Lin W, Huang Y, Chen X, Wang H, Teng L. The Essential Factors of Establishing Patient-derived Tumor Model. *J Cancer*. 2021 Jan 1;12(1):28-37. doi: 10.7150/jca.51749. PMID: 33391400; PMCID: PMC7738839.
- (5) Sharp AK, Colston MJ. The regulation of macrophage activity in congenitally athymic mice. *Eur J Immunol*. 1984 Jan;14(1):102-5. doi: 10.1002/eji.1830140119. PMID: 6420167.
- (6) Shultz LD, Schweitzer PA, Christianson SW, Gott B, Schweitzer IB, Tennent B, McKenna S, Mobraaten L, Rajan TV, Greiner DL, et al. Multiple defects in innate and adaptive immunologic function in NOD/LtSz-scid mice. *J Immunol*. 1995 Jan 1;154(1):180-91. PMID: 7995938.
- (7) Chen, A., Neuwirth, I., & Herndler-Brandstetter, D. (2023). Modeling the Tumor Microenvironment and Cancer Immunotherapy in Next-Generation Humanized Mice. *Cancers*, 15(11), 2989. <https://doi.org/10.3390/cancers15112989>
- (8) Liu, Y., Wu, W., Cai, C. *et al.* Patient-derived xenograft models in cancer therapy: technologies and applications. *Sig Transduct Target Ther* **8**, 160 (2023). <https://doi.org/10.1038/s41392-023-01419-2>
- (9) Shultz, L., Brehm, M., Garcia-Martinez, J. *et al.* Humanized mice for immune system investigation: progress, promise and challenges. *Nat Rev Immunol* **12**, 786–798 (2012). <https://doi.org/10.1038/nri3311>
- (10) Tentler, J., Tan, A., Weekes, C. *et al.* Patient-derived tumour xenografts as models for oncology drug development. *Nat Rev Clin Oncol* **9**, 338–350 (2012). <https://doi.org/10.1038/nrclinonc.2012.61>
- (11) Hidalgo, M., et al. (2014). Patient-derived xenograft models: an emerging platform for translational cancer research. *Cancer Discovery*, 4(9), 998–1013.  
<https://doi.org/10.1158/2159-8290.CD-14-0001>