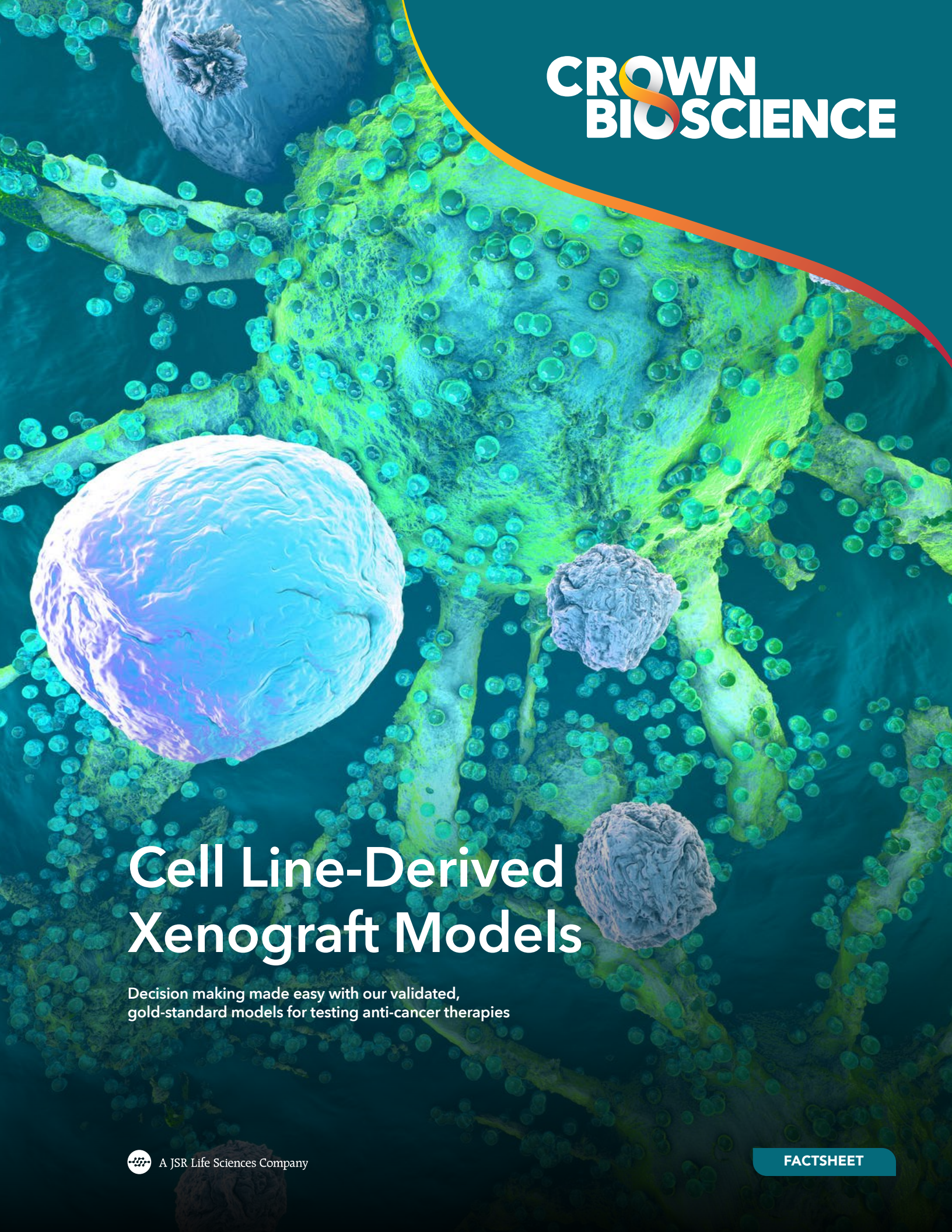


CROWN BIOSCIENCE

# Cell Line-Derived Xenograft Models

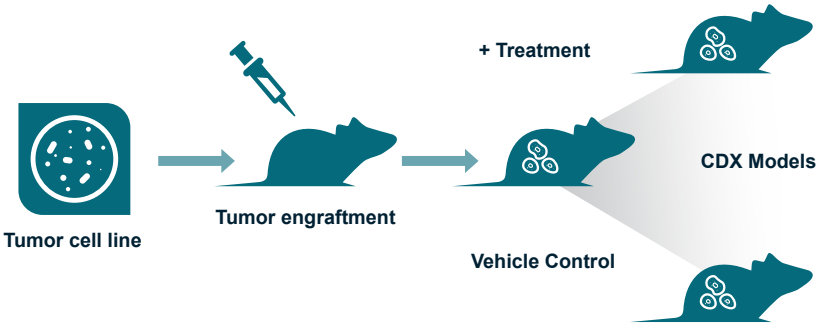
**Decision making made easy with our validated, gold-standard models for testing anti-cancer therapies**

A JSR Life Sciences Company

FACTSHEET

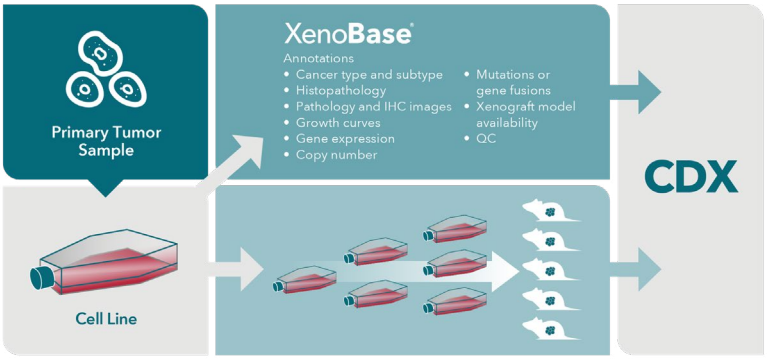
As an integral step in the oncology drug discovery process, cell line-derived xenograft (CDX) models provide key decision-making insights into drug sensitivity, cell biology and signalling pathways in a timely and cost-effective manner.

Crown Bioscience has established multiple *in vivo* assay systems to evaluate novel anticancer compounds, with each assay specifically designed to understand a drug's mechanism of action, or an individual agent property.



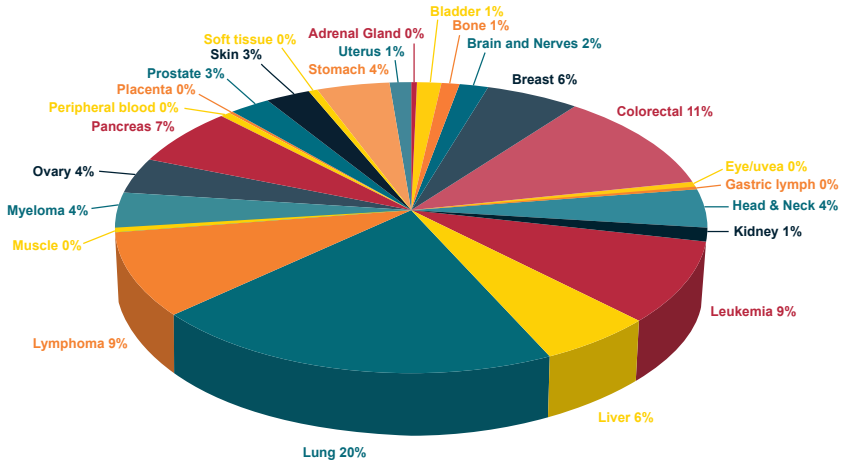

## Determine Your Models of Interest

Working with Crown Bioscience gives you access to **XenoBase®**, our unique online database of well-characterized cell lines and CDX models, which includes standard of care and RNA-seq data to enable simple and rapid model selection.




## Validated CDX Collection

Our collection hosts over 200 validated and well-characterized CDX models covering subcutaneous, orthotopic, and systemic models. The collection includes 25 cancer types, including metastasis models (spontaneous and experimental) covering major cancer types such as: Breast, colon, liver, lung, melanoma, ovarian, pancreatic and prostate, all searchable in our **XenoBase®** database.




## CDX Collection Derived from PDX Models: PrimeXeno™ Models

These unique models are derived from our **HuPrime®** PDX models, via cell lines. Many of these models harbor mutations of novel therapeutic targets, such as: ALK, FGFR2, and FLT3 and R-spondin (RSPO3). **PrimeXeno** models are ideal for early stage drug discovery, where a robust system is needed to screen large numbers of compounds in assays such as PK/PD analysis.

## CDX Models for *In Vivo* Imaging

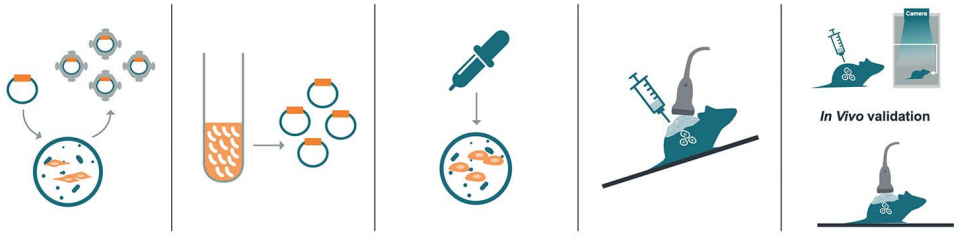
### Bioluminescent Models

Crown Bioscience provides bioluminescent subcutaneous, orthotopic, and metastatic CDX models for optical imaging. These models provide valuable disease information at different cancer stages, through orthotopic models mimicking primary lesions, to the imaging of both spontaneous and experimental metastases to replicate progression to late stage disease.

### Ultrasound Models

Utilize our ultrasound imaging to track disease progression and metastasis. Unlike bioluminescent imagine, high-frequency (HF) ultrasound imaging does not require the use of bioluminescently tagged tumor models. This can reduce study lead time and eliminates the potential of loss-of signal due to necrotic tumor tissue in certain tumor types. Additionally, HF ultrasound offers 2D and 3D imaging for tumor tracking and precise measurement of tumor volume and location.

**Ultrasound guided injection with bioluminescent and/or ultrasound imaging**




### Specialty and Custom Xenograft Models

Crown Bioscience offers additional specialty models and custom model creation for all our client oncology drug discovery and development needs. Custom xenografts and syngeneic models are generated in mice from client mutated/novel cell lines, with QC data and growth kinetics provided for each new model, allowing rapid study initiation. Specialty models available:

- **Dual xenograft models:** Validated pairs of models that may be engrafted on the same mouse without interfering with each other's growth, used for assessing the selectivity of targeted agents.
- **Engineered *in vivo* models:** BaF3-EML4-ALK-WT and the paired, engineered BaF3-EML4-ALK-L1196M as well as BaF3-BCR-ABL-T315I available*
- **CRISPR engineered models:** Global CRISPR licenses enable you to model diseases using stable knockouts/knock-ins and test drug efficacy. To address the challenge of resistance in $KRAS^{G12C}$ inhibitor therapies for NSCLC, we developed $KRAS^{G12C}$ inhibitor resistant tumor models. Using CRISPR/Cas9, secondary KRAS mutations were introduced to analyze growth rates and resistance profiles.

Downstream characterization of *in vivo* models can also be performed using a variety of assay endpoints and techniques, including RNA-Seq, WES, PK/PD, target validation, and efficacy studies.

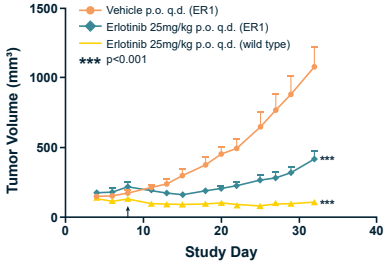
*BaF3 cell lines must be licensed directly by clients

### Drug-Resistant CDX Models for Preclinical Efficacy Testing

CDXs are highly suitable for developing important *in vivo* drug-resistant models. For instance, first-generation EGFR-TKI-resistant models were developed by establishing a drug-resistant cell line by *in vitro* selection. These cells were then used to establish a drug-resistant CDX *in vivo* model.

- Specifically, the HCC827 (NSCLC EGFR tyrosine kinase deletion) cell line was repeatedly challenged with increasing concentrations of erlotinib or gefitinib, resulting in two resistant cell lines (HCC827-ER1 and HCC827-GR1).
- Characterization of these new cell lines showed that both had increased copy numbers of c-MET and expression of Axl compared to the parental HCC827 cells. *In vivo* validation of drug resistance was confirmed by subcutaneously implanting the HCC827-ER1 cell line into nude mice (MF1-nu/nu).
- Erlotinib was very effective in inhibiting tumor growth in "wild-type" cells (yellow plot) but much less effective in preventing the growth of the HCC827-ER1 CDX (blue plot).

***In vivo* validation of the HCC827-ER1 drug-resistant cell line**




## Get in touch

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