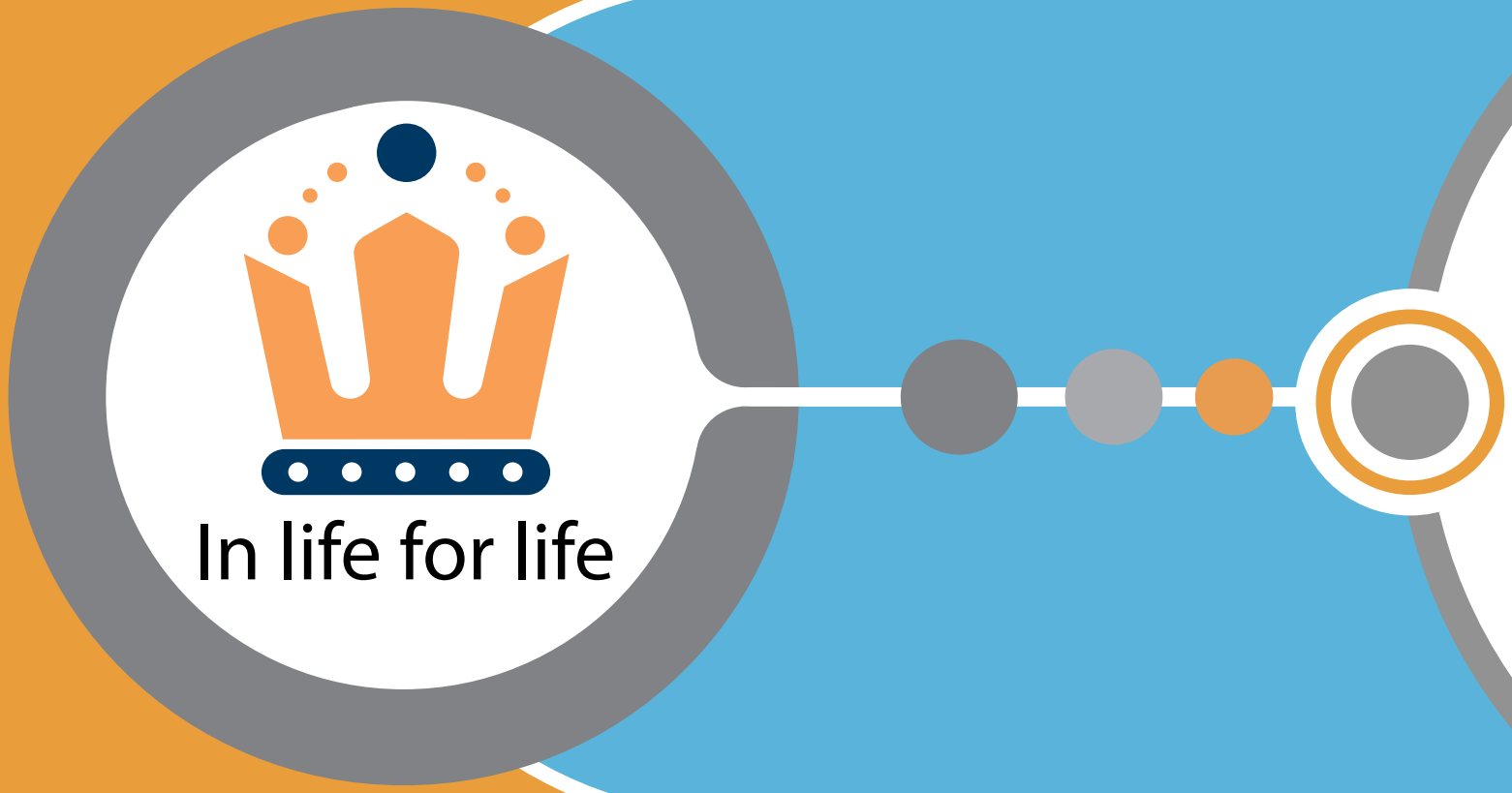
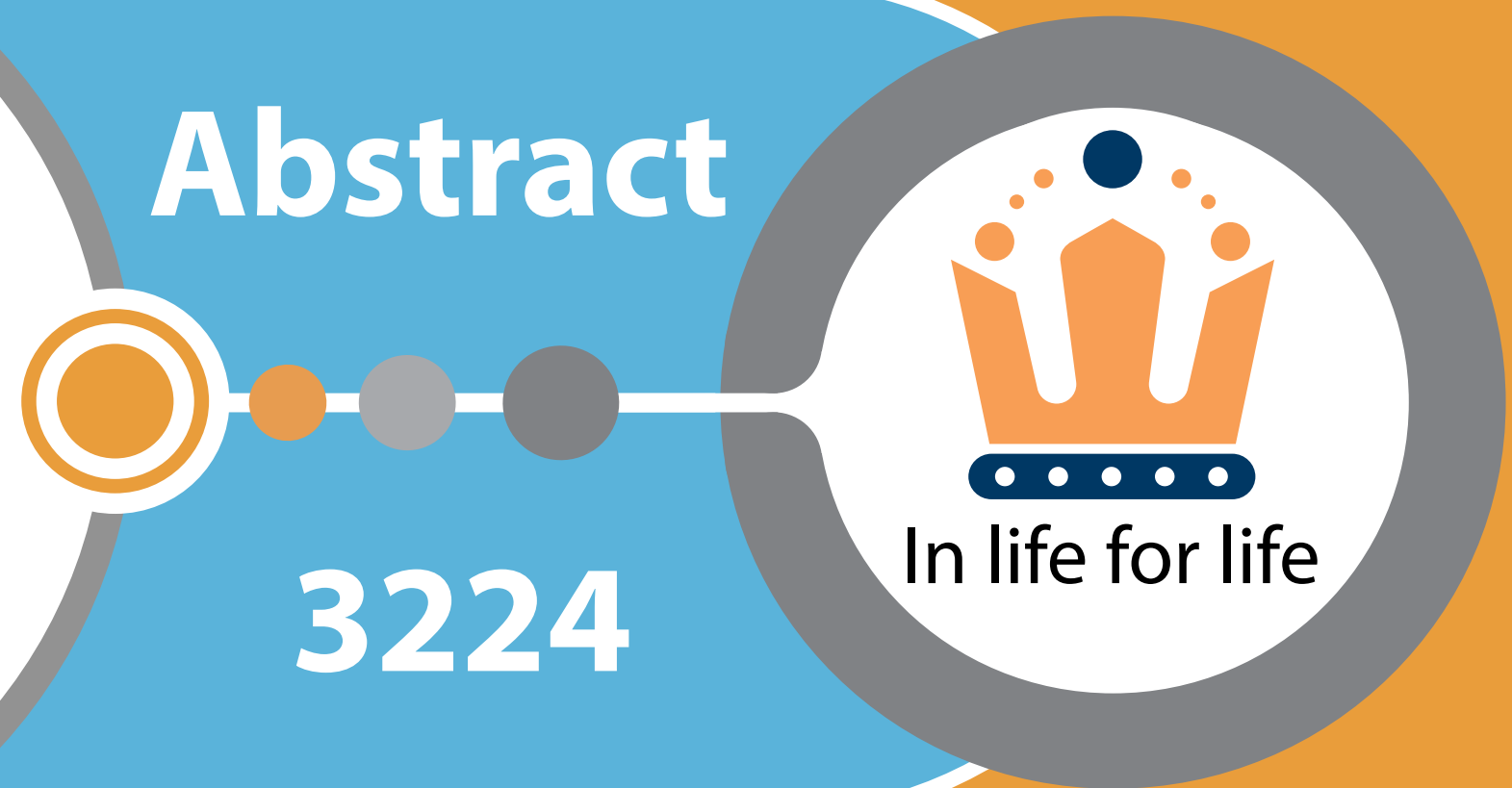




Living Tumor Bank and Patient Derived Xenograft Models: A powerful translational engine for novel oncology therapeutics

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Abstract

Patient-derived xenograft (PDX) models have been established from the world's largest living tumor bank at Molecular Response and used to mimic clinical trial settings with patients from diverse populations and heterogeneous disease; these models are being used to test novel compounds in a more predictive preclinical setting. Overall, the collection is comprised of 144,000 tumor samples corresponding to 70,000 unique patients, and includes >350 PDX models.

Crown Bioscience acquired these PDX models and has exclusive CRO access to the Molecular Response living tumor bank. For several patients, multiple samples were collected at different times (before and after treatment) or at different locations (primary/ metastatic). This allows evaluation of drug efficacy in pre and post treatment application which mimics a clinical setting as well the ability to monitor the effect of drug on the primary tumor and a matched metastatic tumor.

With the addition of the MRL PDX models, Crown Bioscience currently has over 1,600 PDX models established in >70 indications. Validated PDX models have confirmed histology and mutational profiling (Next-Gen sequencing) to demonstrate preservation of biological characteristics between tumor model and patient, as well as between growth passages of the model. Crown's vast and diverse collection of patient derived models allows clients the ability to perform preclinical trials with well-defined patient populations featuring the clinical, histologic, and genomic diversity encountered in the clinic.

HuPrime: >1,600 PDX Models

Cancer Type	Established	Cancer Type	Established
ALL	16	Liver - HCC	99
AML	4	Liver - Other	47
Adrenal	2	Lung - NSCLC	214
Bladder	16	Lung - SCLC	64
Brain Tumor	9	Lung - Other	53
Breast	40	Lymphoma - HL	2
Cervical	16	Lymphoma - NHL	7
Cholangiocarcinoma	21	Lymphoma - Other	14
Colorectal	284	Melanoma	22
Endometrial	1	Neuroendocrine	8
Esophageal	42	Ovarian	53
Fallopian	1	Pancreatic	118
Gallbladder	9	Sarcoma	12
Gastric	177	Testis	1
GIST	5	Thyroid	7
Head & Neck	81	UPS	19
Kidney	15	Uterine Sarcoma	16

Figure 1. The Crown Bioscience HuPrime PDX collection features more than 1,600 models, covering 70 clinical diagnoses

HuPrime: Diverse PDX Models

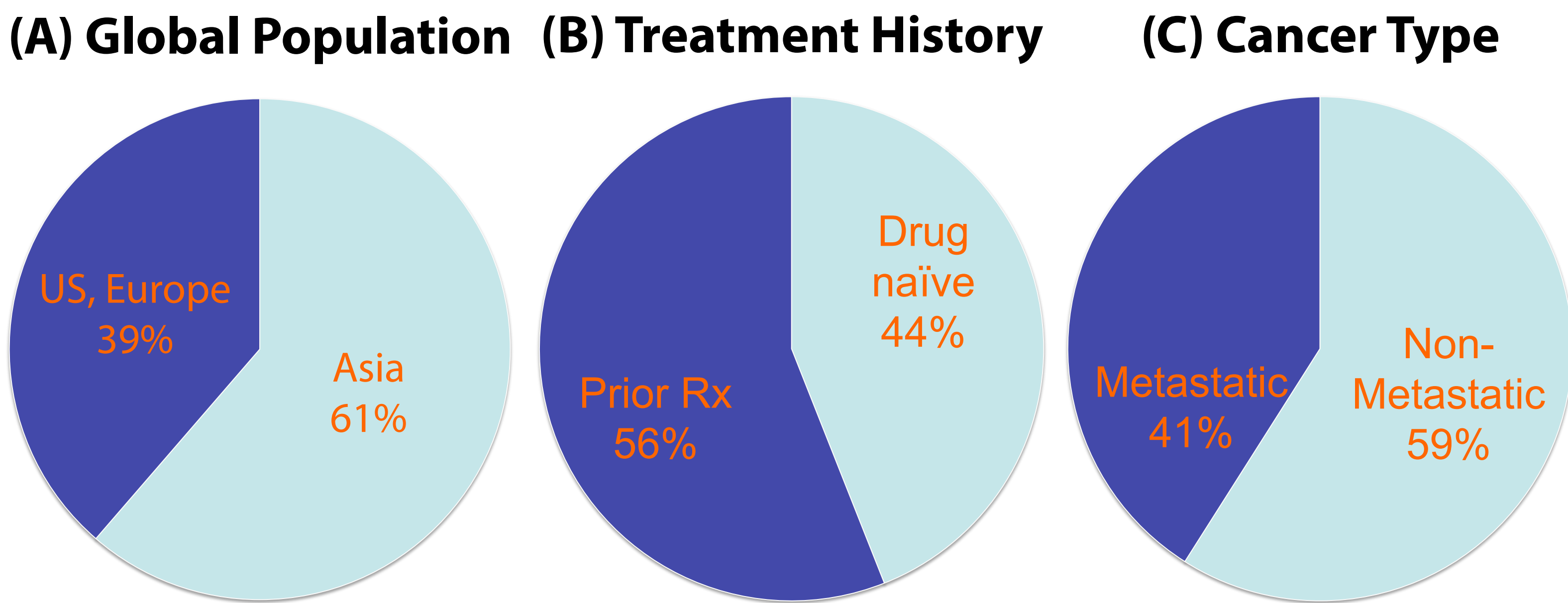


Figure 2. Diverse patient background allows selection of PDX populations representative of clinical populations targeted. (A) HuPrime PDX models represent geographic diversity including models from Asia and non-Asian countries. (B) Within the US/Europe PDX collection, a broad diversity of treatment history as well as (C) cancer stages are represented.

NSCLC: Representative of Clinic

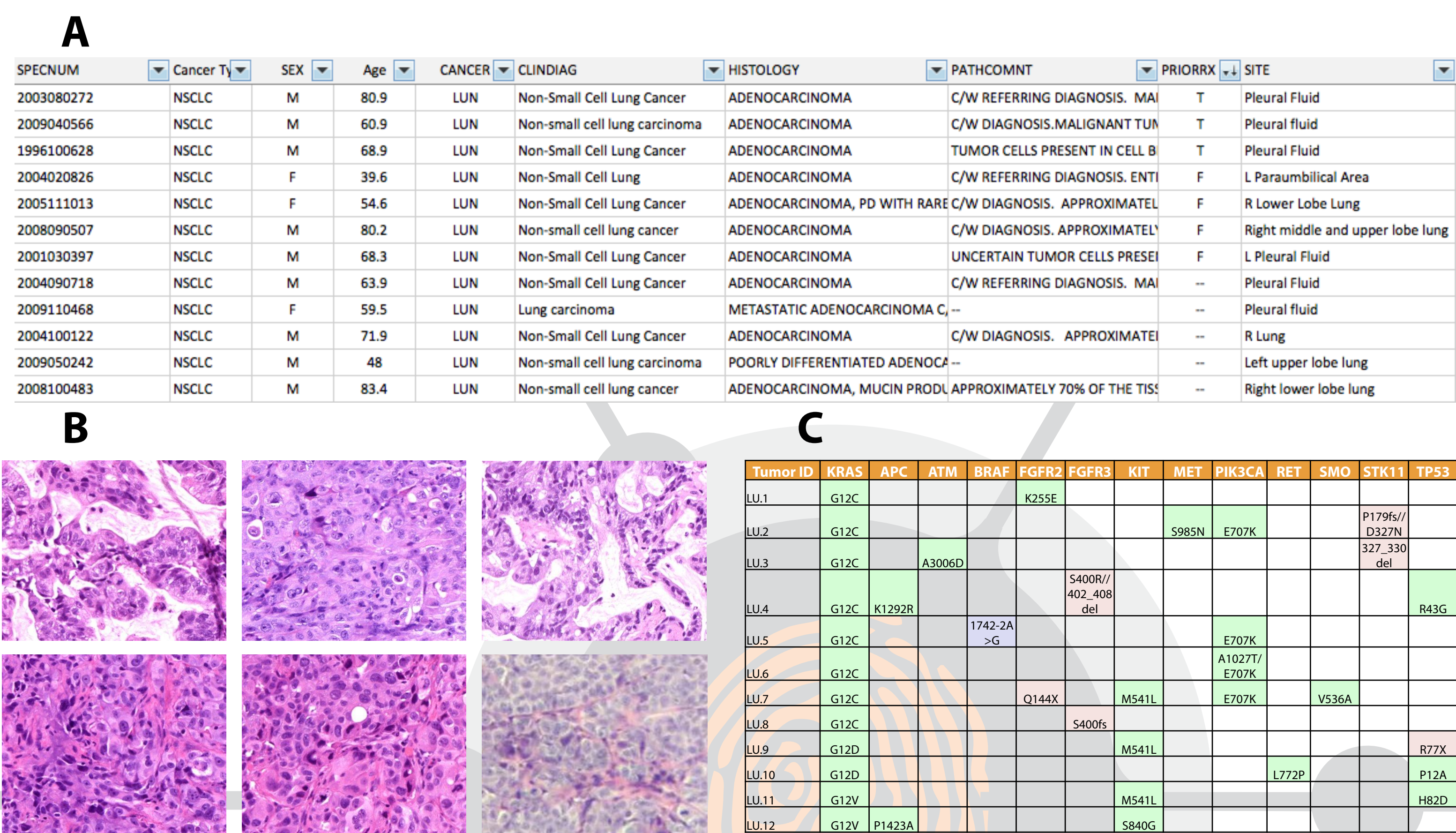


Figure 3. Patient to patient heterogeneity within population of n=12 NSCLC adenocarcinoma KRAS G12 mutant HuPrime PDX models. (A) Despite commonalities within the NSCLC population, variability is observed in clinical parameters. (B) Varied patient histologies seen within population of adenocarcinomas. (C) Mutational profile varies across population of similarly defined NSCLC adenocarcinoma KRAS G12 mutant tumors

NSCLC: Preclinical Trial

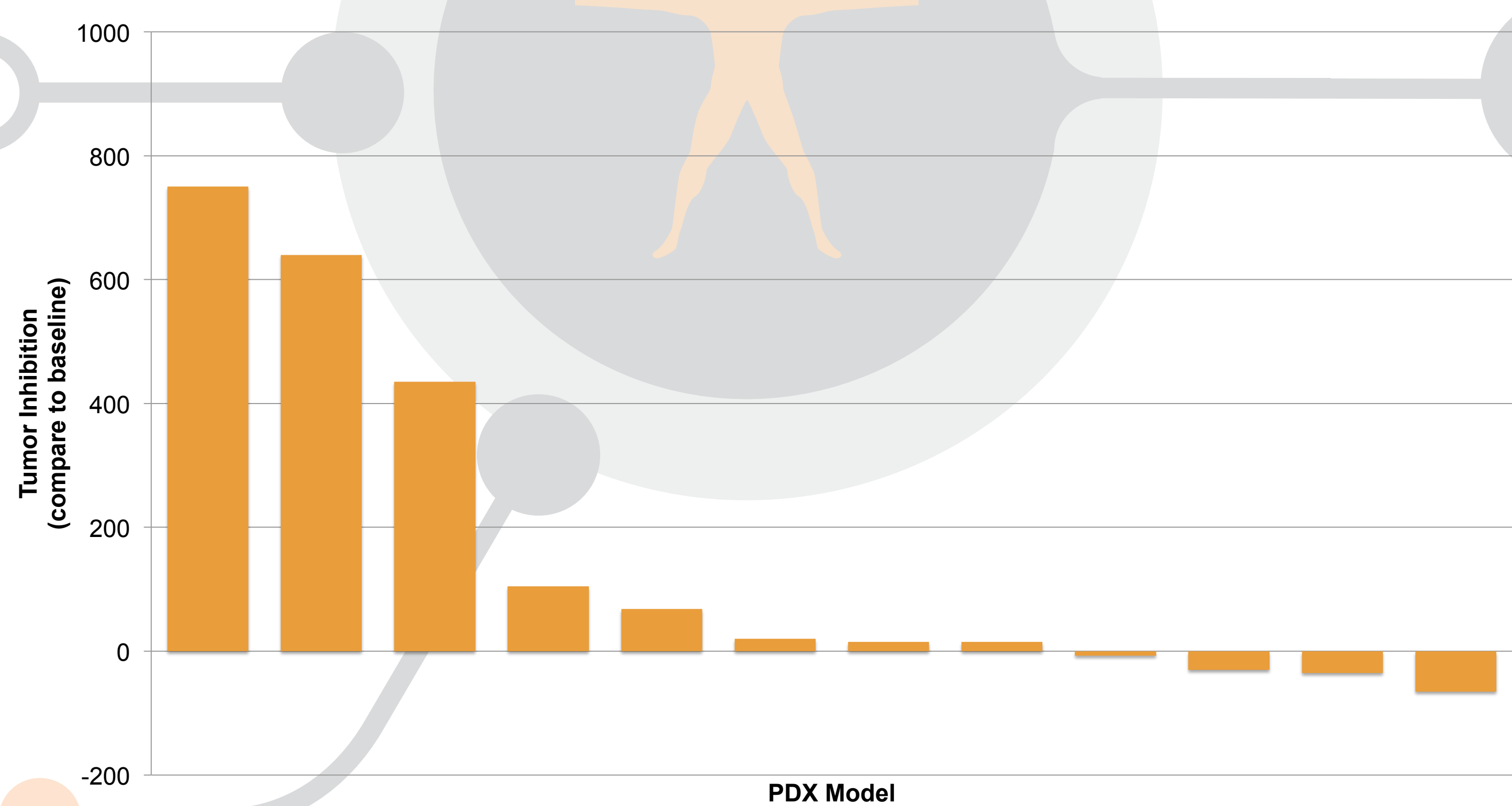


Figure 4. Preclinical Trial in Diverse Patient Background. Drug efficacy measured as tumor growth inhibition across a population of n=12 NSCLC similarly-defined patient derived tumor models. Each column in the waterfall plot represents a patient. 9 of 12 patients observed a growth inhibition or regression effect following treatment, indicating a successful patient selection criteria, despite the heterogeneity represented in the population.

Conclusions

- World's largest & most diverse PDX collection
 - >1,600 PDX Models
- Mirror global clinical population
 - Geographic: Asia, Europe, US
 - Clinical: Late stage, metastatic, prior treated
 - Biomarker: Mutational diversity captured and NGS characterized
- Rapid & On-demand PDX Growth
 - Access to 144,000 'Living Tumor Bank' enables rapid studies of cancer populations
 - Development path of 1,000s PDX models per year
 - Client driven/sponsored PDX creation
- Population studies enable confident preclinical rational for clinical development strategy
 - Patient selection criteria
 - Biomarker/companionDx
 - Combination therapies
 - Candidate prioritization
 - Resistance delay