CrownBio
CONNECTING SCIENCE TO PATIENTS

Corporate Headquarters:
3375 Scott Blvd., Suite 108
Santa Clara, CA 95054
Tel: 855.827.6968
Fax: 888.882.4881
www.crownbio.com

FGFR3-TACC3 Fusion Models

HuPrime® PDX and ValidatedXeno™ CDX Models

FGFR3-TACC3 Fusion Clinical Relevance

- Fibroblast growth factor receptor (FGFR) family of tyrosine kinase receptors are involved in multiple cellular processes
- FGFR3 and transforming acidic coiled-coil containing protein 3 (TACC3) fusion results in increased FGFR3 activation, and has been identified in a range of cancer types e.g. NSCLC, brain tumors, bladder cancer
- FGFR3-TACC3 fusion proteins have been shown to be sensitive to FGFR tyrosine kinase inhibitors (TKIs), providing 'druggable' targets for a selection of cancer patients
- Appropriate preclinical models are needed for evaluation of new targeted treatment options, and for research into the functional capabilities of FGFR3-TACC3 fusion

CrownBio FGFR3-TACC3 Fusion Resources

- CrownBio FGFR3-TACC3 fusion resources include:
  - HuPrime BN2289 glioma and LU6426 NSCLC PDX models
  - Subcutaneous and orthotopic RT112/84 bladder cancer ValidatedXeno CDX models
  - Rat subcutaneous RT112 CDX model
- Our models are sensitive to FGFR inhibitors and show a range of responses to respective SoC treatments
- FGFR inhibitor and SoC agent resistant models and cell lines developed
- All available model information can be found within our curated online PDX (HuBase™) and CDX (XenoBase®) databases
- Expertise and proven track record

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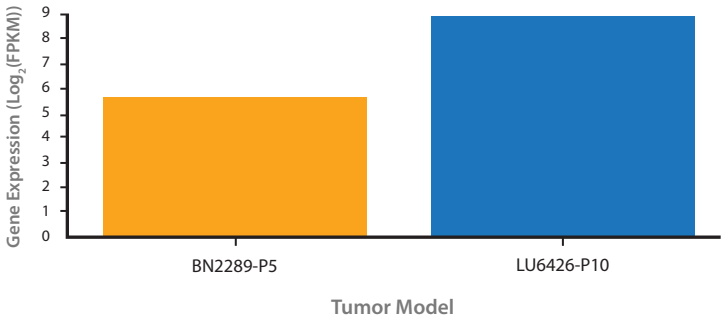
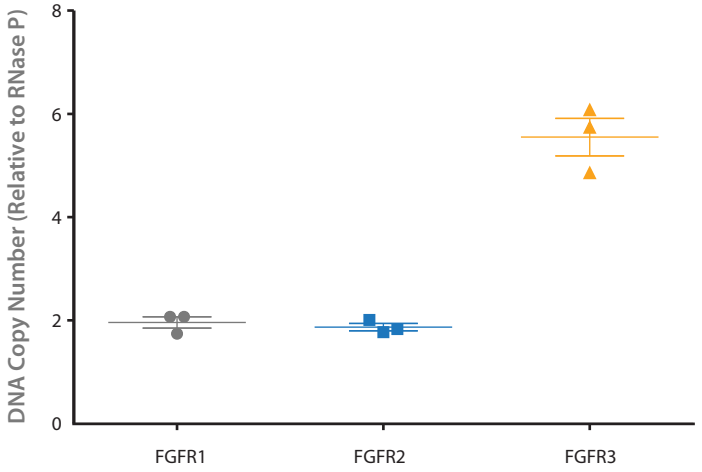
FGFR3-TACC3 Fusion HuPrime Models

Model Characterization and Response to Therapy

HuPrime FGFR3-TACC3 Fusion Model Characterization

HuPrime ID	Patient Background	Tumor Pathology Diagnosis	PDX Tumor Pathology QC	Genomic Profiling	Treatment History	Mutation Status	Background & Model Type
BN2289	Asian patient, aged 75 years	Anaplastic oligodendrogliomas (WHO Grade 3). IHC results: GFAP(+), S-100(+), Syn(-), Ki-67(10% +), MMP-9(-), MGMT(-), P53(-), PCNA(+), P170(+)	Pa, P2: Oligodendrogliomas, Grade 3	P2: Affy U219 P1: Affy SNP 6.0 P5: RNAseq	Naive	WT: AKT, BRAF, CTN-NB1, EGFR, KRAS, MAPK1, PIK3CA MYC amplified	BALB/c nude mice. Subcutaneous and orthotopic
LU6426	Caucasian patient, aged 80 years, smoker	NSCLC, SCC	P11: Poorly differentiat-ed squamous cell carcinoma	P10: RNAseq	Naive	WT: KRAS, LKB1, EGFR Mutation: TP53 R158L	MF-1 nude mice, hMSC supplement; BALB/c nude mice. Subcutaneous



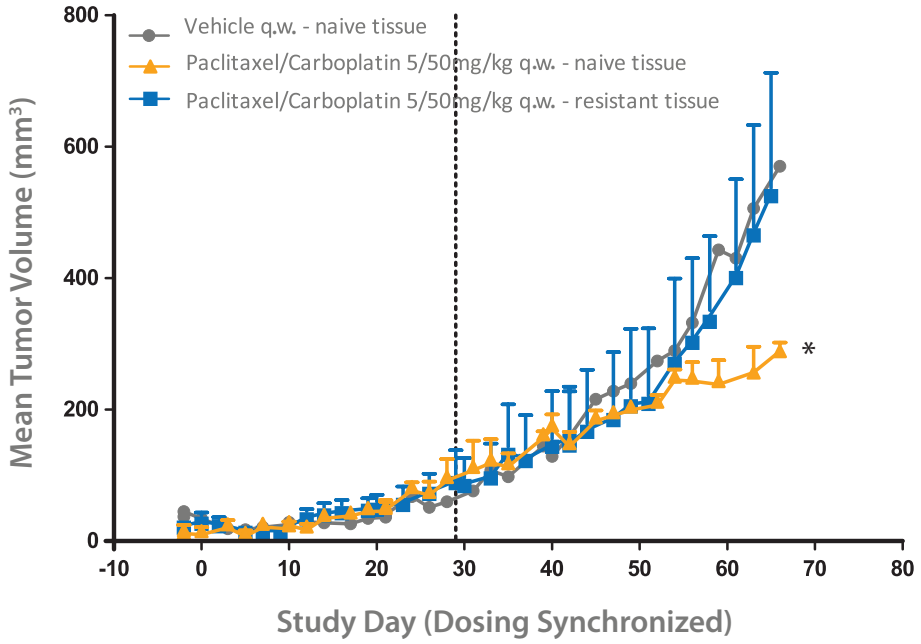


HuPrime FGFR3-TACC3 Fusion Model Treatment Data

Model	Radiotherapy		Targeted Therapy		Chemotherapy	
	Resistant	Sensitive	Resistant	Sensitive	Resistant	Sensitive
BN2289 (BALB/c nude mice)	-	-	-	BGJ398 (FGFR inhibitor)	-	Temozolo-mide
LU6426 (MF-1 nude mice)	-	24Gy fractionated dose	-	AZD4547 (FGFR inhibitor)	Paclitaxel + carboplatin (acquired resistance)	Paclitaxel + carboplatin

HuPrime LU6246 Model Response to SoC and Acquired Resistance

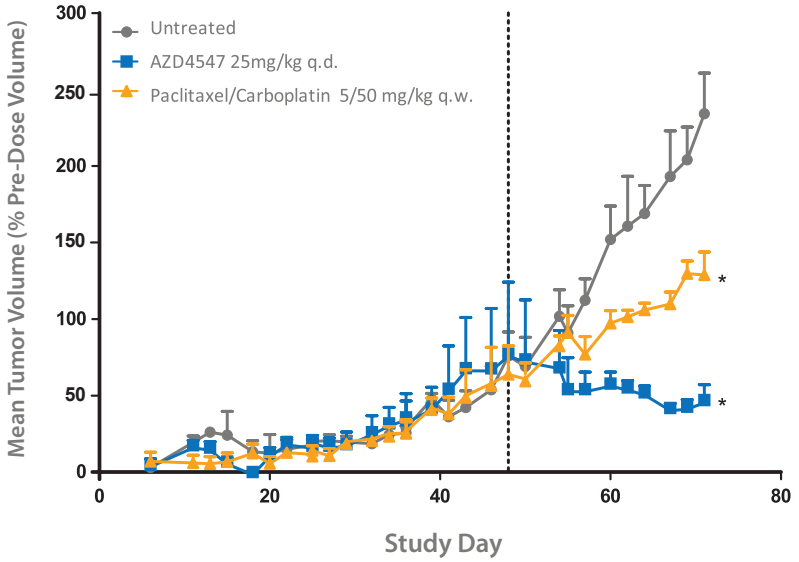
- LU6426 is sensitive to paclitaxel and carboplatin combination therapy (*p≤0.001)
- An LU6426 model of acquired resistance to paclitaxel and carboplatin has been developed through cycled dosing *in vivo*



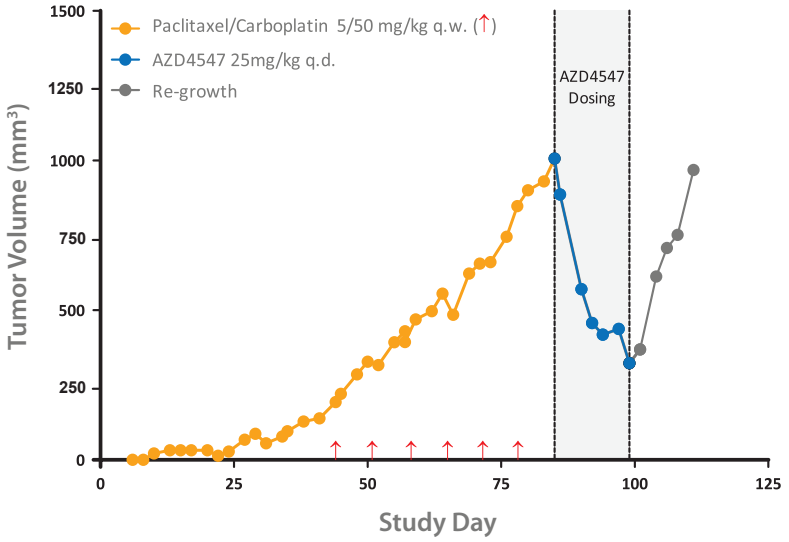
HuPrime LU6246 Model Response to FGFRi

- LU6426 is sensitive to FGFR inhibitor treatment, with the response maintained in the acquired chemotherapy resistance setting

LU6426 model is sensitive to AZD4547 and paclitaxel/carboplatin treatment (*p≤0.001)

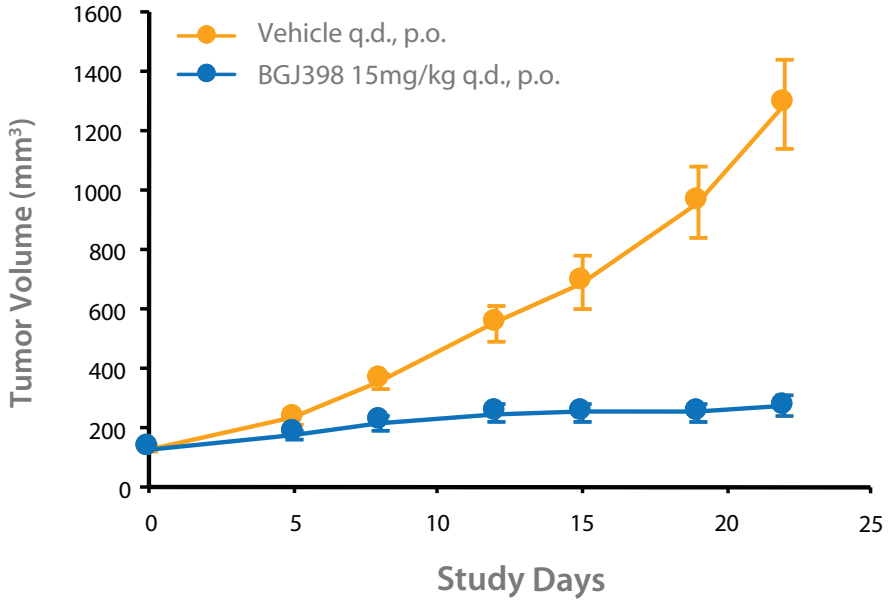


LU6426 model is sensitive to AZD4547 in acquired paclitaxel/carboplatin resistance setting



HuPrime BN2289 Model Response to FGFRi

- BN2289 is sensitive to treatment with the pan FGFR inhibitor BGJ398



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FGFR3-TACC3 Fusion ValidatedXeno RT112/84 Model

Model Characterization and Response to Therapy

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SYDNEY

ValidatedXeno RT112/84 Model Background and Treatment Data

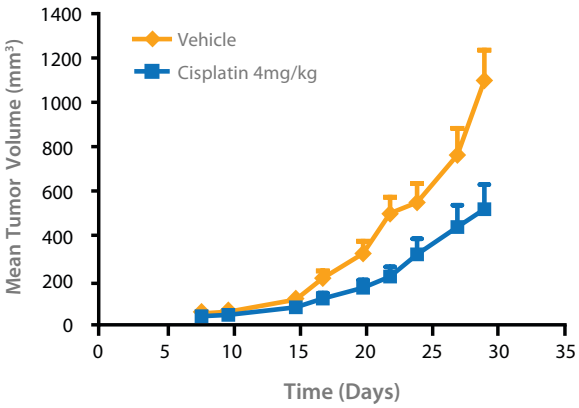
Model	Cancer Type	Model Type	Model Information	Background
RT112/84	Urinary tract; bladder	Subcutaneous, orthotopic, and bioluminescent	A human female epithelial bladder carcinoma, which is tumorigenic in nude mice. A clonal derivative of the RT112 cell line[12,13]	MF-1 female nude mice, NOD/SCID, BALB/c nude

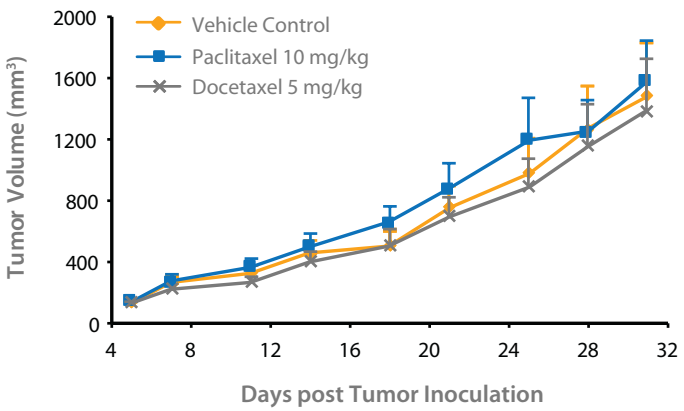
Model	Targeted Therapy		Chemotherapy	
	Resistant	Sensitive	Resistant	Sensitive
RT112/84 Subcutaneous	AZD4547 (FGFR inhibitor) resistant model being generated	Lucitanib, lenvatinib, sunitinib. Regression/ stabilization with AZD4547 (FGFR inhibitor)	Docetaxel, paclitaxel	Partial response with cisplatin

ValidatedXeno RT112/84 Model Response to SoC

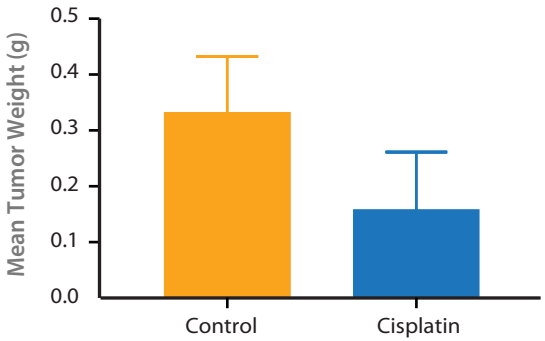
- RT112/84 subcutaneous and orthotopic models show partial response following cisplatin treatment
- The subcutaneous RT112/84 model is resistant to paclitaxel or docetaxel treatment

RT112/84 Subcutaneous Model Response to Chemotherapy



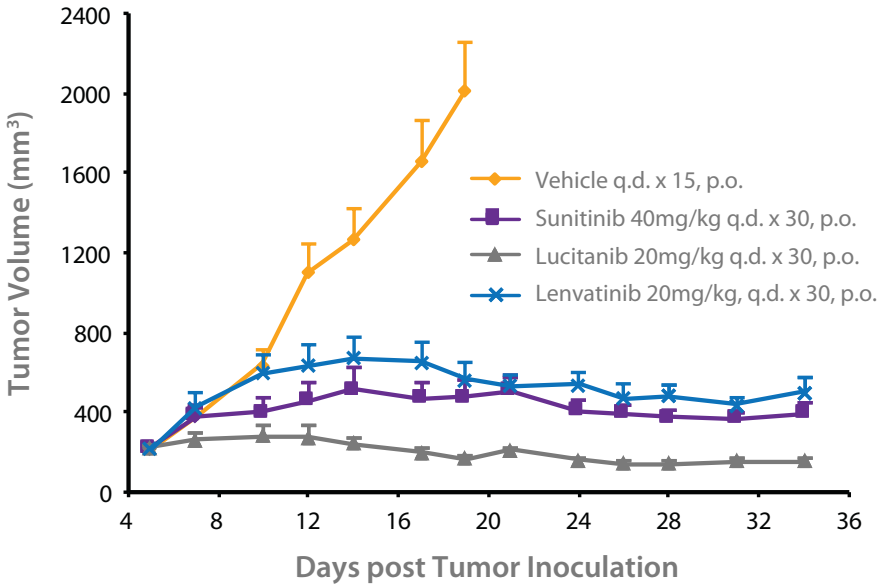


RT112/84 Orthotopic Model Response to Cisplatin



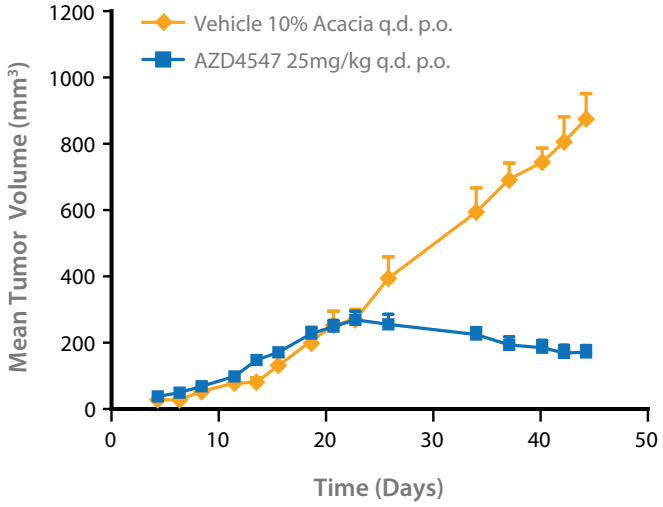
ValidatedXeno RT112/84 Model Response to TKIs

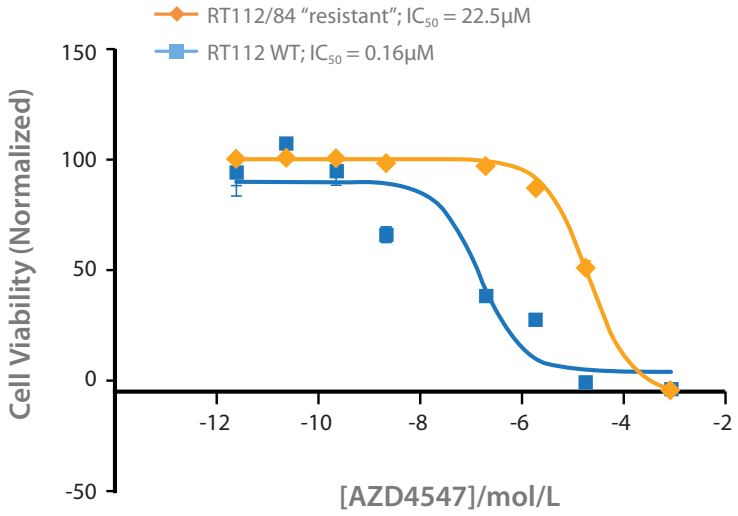
- The RT112/84 model is sensitive to sunitinib, lucitanib, and lenvatinib



Model Response to FGFRi and Development of Resistance

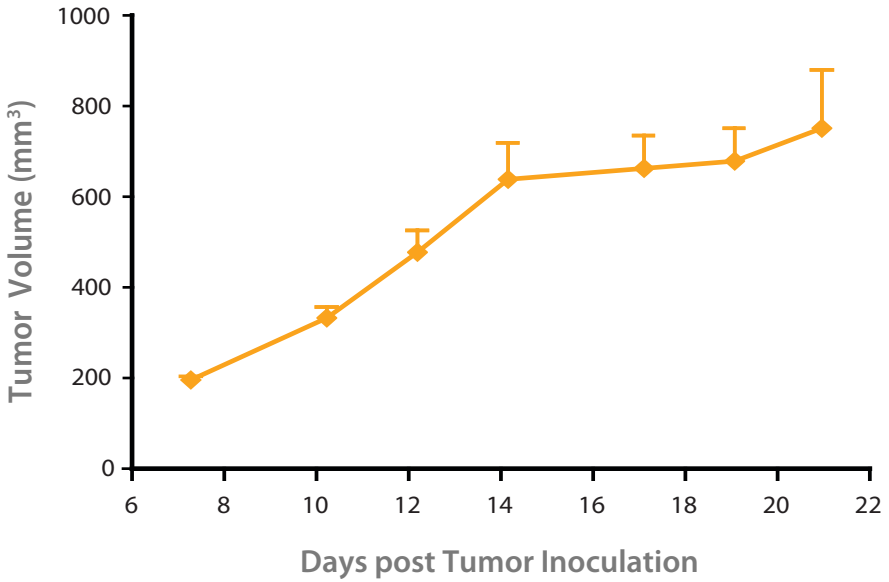
- RT112/84 is highly sensitive to the FGFRi AZD4547
- *In vitro* resistance to AZD4547 has been established, with the resulting model available for *in vivo* validation studies





RT112 Subcutaneous Rat Model

- CrownBio has also established a nude rat model from the parental RT112 cell line



Summary

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Connect with CrownBio

- Contact us at **busdev@crownbio.com** for full details on our FGFR-TACC3 Fusion models
- Explore CrownBio models through our online databases
- One stop search for PDX, CDX, syngeneics with Onco*Express*™ at **oncoexpress.crownbio.com**
- Or investigate PDX models in HuBase, CDX models via XenoBase, accessible from **www.crownbio.com**