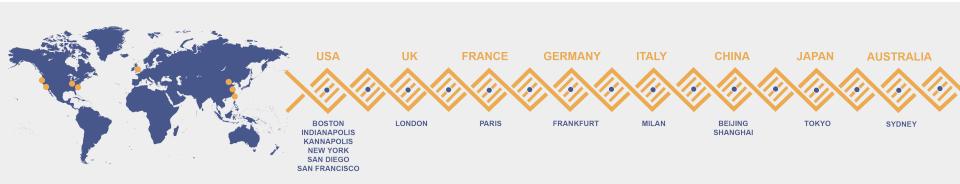


Corporate Headquarters:

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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

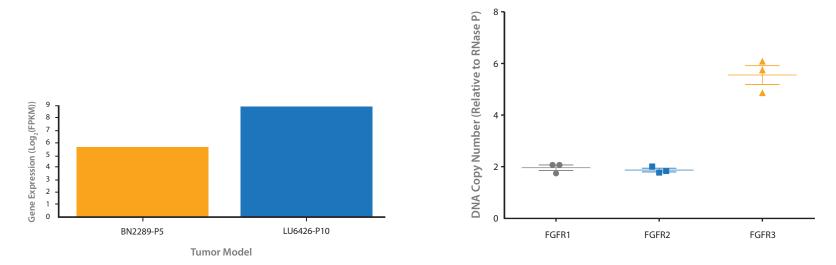
Model Characterization and Response to Therapy





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



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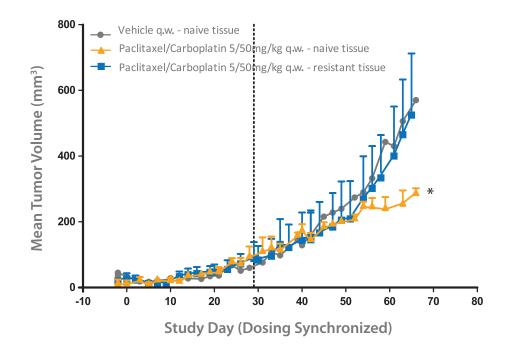
HuPrime FGFR3-TACC3 Fusion Model Treatment Data

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*



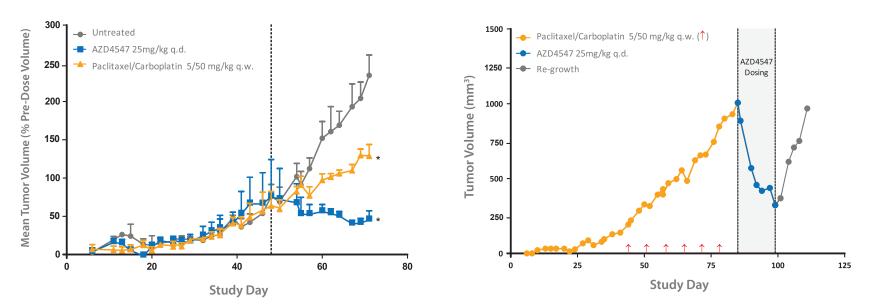


HuPrime LU6246 Model Response to FGFRi

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)

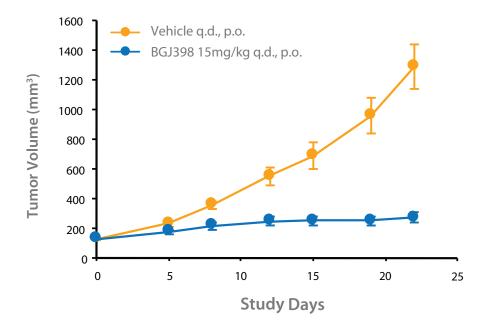
LU6426 model is sensitive to AZD4547 in acquired paclitaxel/carboplatin resistance setting





HuPrime BN2289 Model Response to FGFRi

BN2289 is sensitive to treatment with the pan FGFR inhibitor BGJ398



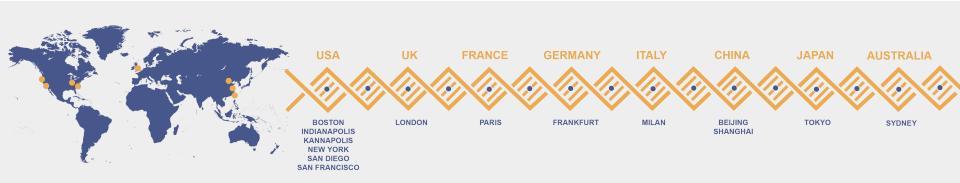


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FGFR3-TACC3 Fusion ValidatedXeno RT112/84 Model

Model Characterization and Response to Therapy





ValidatedXeno RT112/84 Model Background and Treatment Data

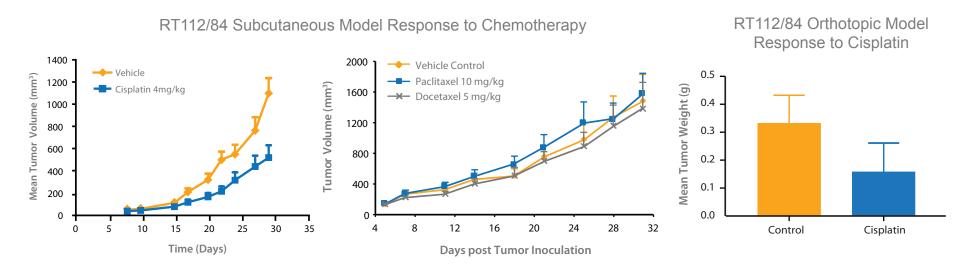
Model	Cancer Type	Model Type	Model Information	Background
RT112/84	Urinary tract; bladder	Subcutaneous, orthotopic, and bioluminescent	A human female epithelial bladder carcinoma, which is tumorigenic in nude mice. A clonal derivative of the RT112 cell line ^(12,13)	MF-1 female nude mice, NOD/SCID, BALB/c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

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



ValidatedXeno RT112/84 Model Response to SoC

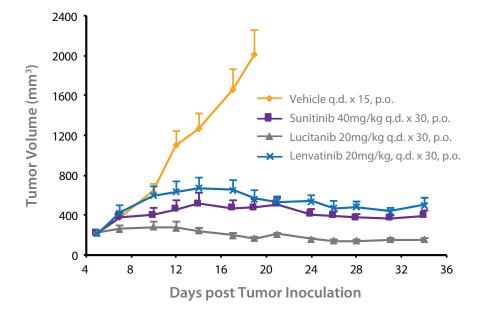
- RT112/84 subcutaneous and orthotopic models show partial response following cisplatin treatment
- The subcutaneous RT112/84 model is resistant to paclitaxel or docetaxel treatment





ValidatedXeno RT112/84 Model Response to TKIs

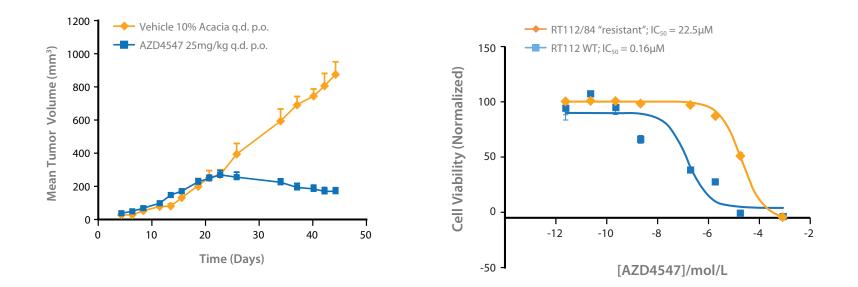
 The RT112/84 model is sensitive to sunitinib, lucitanib, and lenvatinib





Model Response to FGFRi and Development of Resistance

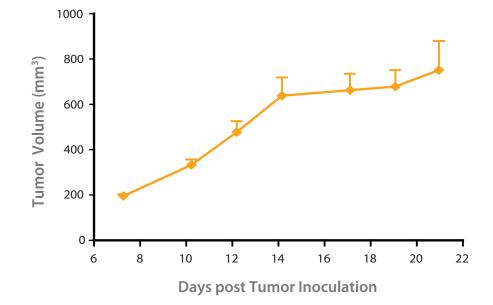
- RT112/84 is highly sensitive to the FGFRi AZD4547
- In vitro resistance to AZD4547 has been established, with the resulting model available for *in vivo* validation studies





RT112 Subcutaneous Rat Model

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







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- Expertise and proven track record



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 OncoExpress™ at oncoexpress.crownbio.com
- Or investigate PDX models in HuBase, CDX models via XenoBase, accessible from www.crownbio.com





FGFR3-TACC3 Fusion FactSheet FGFR3-TACC3 fusion oncogenes are important targets for oncology research

The Abrobiast growth factor receptor FGFR lamily of tyrosine kinase receptors are involved in a wide range of cellular activities including proliferation, differentiation, and unrival. Mutations, single nucleatide projencephane (MPM), amplifications, and translocations of family members CFRT fit herough FGFR the been implicated as casbidly and the second in a action control of the second second

The functional capabilities of FGRID NGC1 facios proteins are summity being inverginal Ganas, Markag and Inog annor collabilitis regimes (FGRID-SEC) facios proteins, have been thours to instrument of a patient with critical carcon carrying the GRID-SEC facios with a multi-factors. The targeting FGRI also collection is static descent with critical carcon carrying the GRID-SEC facion with a multi-factors. The targeting FGRI also collection is address on supervised FGRI all factors are also been then entitates to combined EGRI and GRID models has shown their entitates to combined EGRI and GRID factors and any EGRID-SEC factors also parameted apartory.

These treatment responses and enverging data suggest that FGR3-DCC fusions could provide threggable' targets for a selection of cancer patients, and could be the key to treating acquied drug resistance in contraint, accorpticate predicaical models are now needed for evaluation of new aspets, and for further research into the functional canabilities of FCRE-DMC1 foreign.

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