

DRUG DISCOVERY INITIATIVE TOOLBOX SUBMISSION FORM

Your Contact Information

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May we list your name & institution/company/affiliation in the online Toolbox listing?

<input type="checkbox"/> NO - please list anonymously
<input checked="" type="checkbox"/> YES - you may list my name & institution/company/affiliation

Tool Type Submitted

Tool Type
<input type="checkbox"/> In vitro model
<input type="checkbox"/> In vivo model
<input checked="" type="checkbox"/> Candidate therapeutic
<input type="checkbox"/> Drug delivery technology
<input type="checkbox"/> Other _____

How did you learn about DDI?

- CTF website
 CTF NewsBlast
 CTF booth at convention

Other (describe) _____

Page:

Tool Type: Details

Check as many as apply

Relevant to Disorder	Screening Models	Therapeutic Focus within NF	Signaling pathway/target
<input checked="" type="checkbox"/> NF1	In vitro models:	<input type="checkbox"/> Plexiform neurofibroma	<input type="checkbox"/> Growth factor receptor modulator
<input checked="" type="checkbox"/> NF2	<input type="checkbox"/> Cell line (human)	<input type="checkbox"/> Neurocutaneous fibroma	<input type="checkbox"/> Ras-dependent
<input checked="" type="checkbox"/> Schwannomatosis	<input type="checkbox"/> Cell line (animal)	<input type="checkbox"/> Schwannoma	<input type="checkbox"/> Ras-independent
<input type="checkbox"/> Other	<input type="checkbox"/> Primary cells (human)	<input type="checkbox"/> Meningioma	<input type="checkbox"/> PI3K
	<input type="checkbox"/> Primary cells (animal)	<input type="checkbox"/> Optic Glioma	<input type="checkbox"/> Raf/MEK/ERK
	<input type="checkbox"/> Mouse models:	<input type="checkbox"/> Astrocytoma	<input type="checkbox"/> Rac 1/2/Rho
	<input type="checkbox"/> Transgenic	<input type="checkbox"/> MPNST	<input checked="" type="checkbox"/> PAK1
	<input type="checkbox"/> Human xenograft	<input type="checkbox"/> PNS Tumors - other	<input type="checkbox"/> mTOR
	<input type="checkbox"/> Other	<input type="checkbox"/> CNS Tumors - other	<input type="checkbox"/> PKCalpha
	<input type="checkbox"/> Animal models - other:	<input type="checkbox"/> Dysplasia/Bone Defects	<input type="checkbox"/> Other _____
	<input type="checkbox"/> Zebrafish	<input type="checkbox"/> Cardiovascular Defects	
	<input type="checkbox"/> Drosophila	<input type="checkbox"/> Cognition/learning	
	<input type="checkbox"/> Other _____	<input type="checkbox"/> Pain	
		<input type="checkbox"/> Blood disorders	
	Candidate therapeutics:	<input type="checkbox"/> Other _____	
	<input type="checkbox"/> Antibody		
	<input type="checkbox"/> Peptide		
	<input type="checkbox"/> Small molecule/chemical entity/array		
	<input type="checkbox"/> Gene therapy		
	<input type="checkbox"/> RNA silencing		
	<input type="checkbox"/> Other _____		

Description of tool:

Afraxis has developed potent ($IC_{50} < 10$ nM) and selective (> 100 -fold against Group 2 PAKs) small molecule inhibitors of PAK1. Lead inhibitors have demonstrated suitable oral availability and pharmacokinetics that are consistent with once a day dosing in mice to provide sustained plasma levels throughout a 24 hour period. The inhibitors have also demonstrated suitable brain penetration that provides sustained brain levels throughout a 24 hour period.

Afraxis inhibitors are available for testing in suitable *in vitro* or *in vivo* models of NF1 and NF2.

The figure below highlights the importance of PAK1 as a downstream signaling target in both NF1 and NF2.

