

Cardio-Renal Disease Polycystic Kidney Disease Program

NOVEMBER 2010

Plexxikon is developing novel, oral kinase inhibitors for the treatment of polycystic kidney disease (PKD).

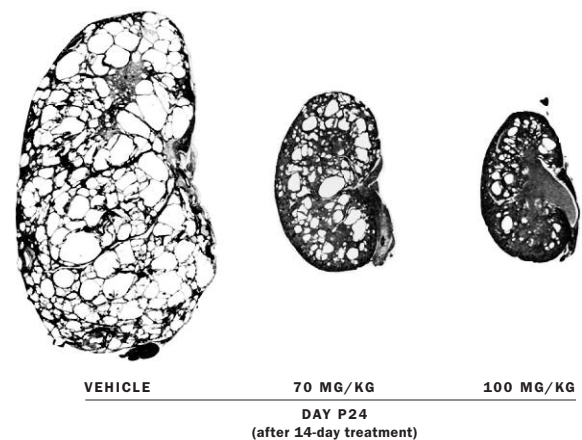
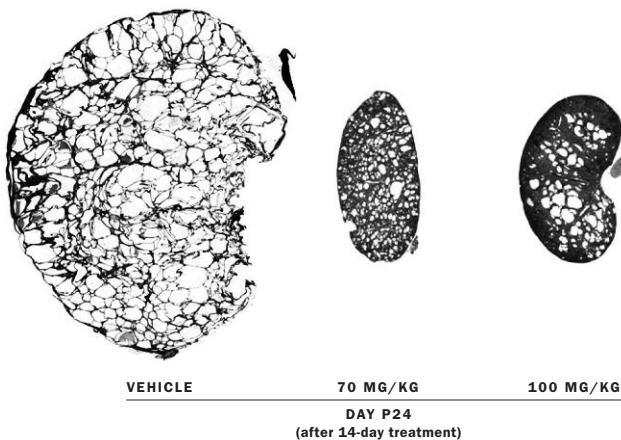
Using its highly selective and potent inhibitors of Raf kinase, Plexxikon has demonstrated compelling efficacy in multiple preclinical models of PKD, and shown that the target Raf kinase is a critical mediator of PKD pathology.

➤ About Polycystic Kidney Disease

PKD is a debilitating genetic disease in which cysts form in the kidneys, causing them to become enlarged and infected, or burst, ultimately leading to loss of kidney function. Currently, there is no treatment for PKD, and patients eventually progress to kidney transplant or dialysis. PKD is the most common life-threatening genetic disease, affecting approximately 600,000 patients in the US and over 12 million worldwide.

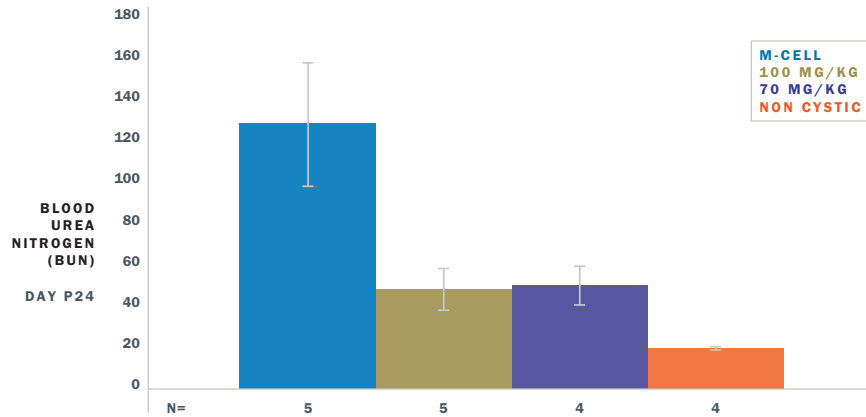
➤ Preclinical Data Demonstrates Dramatic Improvement in PKD

Plexxikon's inhibitors have demonstrated impressive efficacy in orthologous models of both forms of PKD (PKD 1 and PKD 2), including effects on cyst size and renal function.



PLX5568 SIGNIFICANTLY REDUCES KIDNEY CYSTS IN BOTH
PKD1^{FLOX/FLOX}; PKHD1-CRE MICE (LEFT) AND IN PKD2^{FLOX/FLOX}; PKHD1-CRE MICE (RIGHT)

Preclinical Data Shows Improved Kidney Function



Selectivity of Plexikon's Raf Kinase Inhibitors Minimizes Side Effects

Using its proprietary Scaffold-Based Drug Discovery™ platform, Plexikon has identified a portfolio of unique compounds that selectively target a unique binding site of the Raf protein, minimizing the common side effects seen from other less selective kinase inhibitors. In several different systems, Plexikon's Raf inhibitor blocks proliferation of dysfunctional cells, without detectable effects on healthy cells.

Plexikon and 2008 Roche Collaboration Focuses on PKD

In November 2008, Plexikon signed an agreement with Roche to collaborate in the development of selective Raf inhibitors for PKD.



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