

# RX-5902 Exhibits Direct & Immunomodulatory Anti-tumor Activities In Melanoma PDX Models

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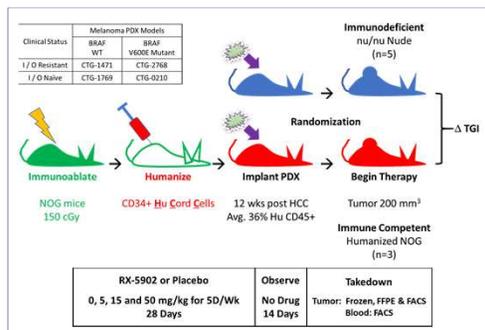
## Background & Methods

**Background:** Nuclear  $\beta$ -catenin promotes deleterious processes in tumors and their microenvironment. Diminishing nuclear  $\beta$ -catenin attenuates these oncogenic processes. RX-5902 is an oral, small molecule inhibitor of  $\beta$ -catenin nuclear translocation mediated by phosphorylated p68 (DDX5). RX-5902 exhibits potent anti-cancer activity in many cancer cell lines, xenograft models in immunodeficient mice and immune competent mice. This study examines the relative contribution and context of the direct and immunomodulatory effects on the anti-tumor activities of RX-5902.



**Methods:** Four patient-derived melanoma xenograft models were implanted into either immunodeficient nude mice or NOG mice "humanized" with HLA unmatched CD34+ stem cells with average humanization of 36%. The PDX models were derived from 2 tumors that were clinically unresponsive to an anti-PD-1 agent and 2 tumors obtained prior to any immune treatment. In each category one tumor had BRAF WT and one a V600E mutation. Mice were randomized to receive either vehicle or RX-5902 at 5, 15 or 50 mg/kg po QDx5/Off x2 when implanted tumors reached 100-120 mm<sup>3</sup> and began treatment when tumors reached 200mm<sup>3</sup>. Treatment lasted for 28 days and animals were observed for an additional 14 off therapy.

## Study Design



## Primary Outcome: Day 28 $\Delta$ TGI

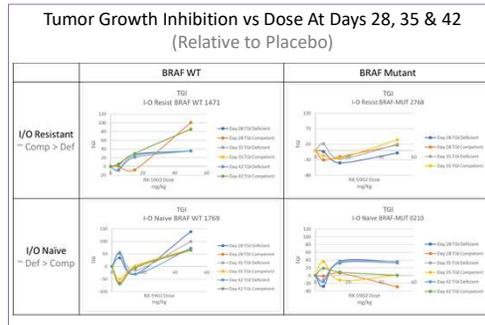
Average Melanoma PDX Tumor Growth Inhibition (%)

Clinical Category	BRAF Status	I/O Resistant		I/O Naive	
		WT	V600E	WT	V600E
Day 28 TGI (On Drug)	Immunocompetent	100	17	67	-29
	Immunodeficient	35	-8	138	36
Day 35 TGI (Off Drug)	Immunocompetent	85	34	70	1
	Immunodeficient	30	20	99	36
Champions Oncology Models		CTG-1471	CTG-2768	CTG-1769	CTG-0210

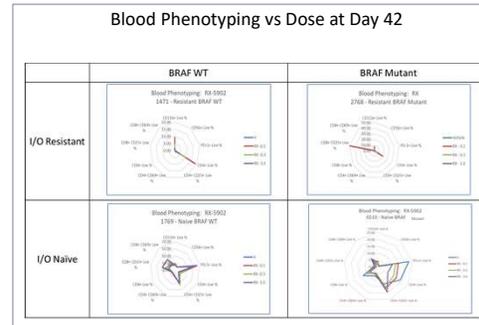
## Conclusions

- RX-5902 has been shown to augment anti-PD-1 immunotherapy in multiple pre-clinical cancer models (syngeneic and humanized), including triple-negative breast cancer, when used in combination therapy.
- This study provides a comparison of tumor growth inhibition ( $\Delta$ TGI) of RX-5902 monotherapy in 4 patient-derived melanoma xenograft (PDX) models in both immune deficient and immune competent mice to identify RX-5902-induced anti-tumor immune activity during and following therapy.
- RX-5902 provided greater tumor growth inhibition ( $\Delta$ TGI) in the two melanoma PDX models derived from subjects who were resistant to I/O therapy compared to the two models from I/O naive subjects.
- TGI is greater in BRAF WT vs BRAF V600E mutant tumors.
- RX-5902 immune-mediated anti-tumoral activity may benefit the majority of melanoma subjects with limited response to BRAF-directed and/or I/O therapy.

## TGI vs RX-5902 Dose



## A Secondary Outcome At Day 42



## Acknowledgements

This study was designed and supported by Rexahn Pharmaceuticals. Work was conducted at Champions Oncology under the direction of Dr. D. Shah and Mr. Lonnie Myer.

