

RP01 for the treatment of Renal Cell Carcinoma

*A therapy at the Intersection of
Systemic Metabolism and Tumor Metabolism*



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The Team



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Science



Melisa Lopez-Anton, PhD
Blavatnik Fellow at Yale University
Scientist in Cancer Biology
Entrepreneur

Entrepreneur / Science



David Lewin, PhD
Director of Business Development
Yale Office of Cooperative Research

Business

High-impact Scientific Publications

ARTICLE **nature** **Cell** Article **Cell**

Acetate mediates a microbiome-brain- β -cell axis to promote metabolic syndrome
Rachel J. Perry,¹ Liang Peng,¹ Natabha A. Barry,^{1,2} Gary W. Cline,¹ Dongyan Zhang,¹ Rebecca L. Cardone,¹ Kim Falk-Petersen,^{1,3} Richard G. Kibbey,^{1,4} & Gerald I. Shulman^{1,2,4*}

Leptin Mediates a Glucose-Fatty Acid Cycle to Maintain Glucose Homeostasis in Starvation
Rachel J. Perry,¹ Yongliang Wang,¹ Gary W. Cline,¹ Aviva Rabin-Cour,¹ & Gerald I. Shulman^{1,2,4*}

Hepatic Acetyl CoA Links Adipose Tissue Inflammation to Hepatic Insulin Resistance and Type 2 Diabetes
Richard G. Kibbey,^{1,2} Dongyan Zhang,¹ Curtis J. Perry,^{1,2} Zhang, He-Sin Huan,¹ Xinyong Yang,^{1,2} et al. Davis,¹ & Gary W. Cline¹

Cell Reports Report **Science**

Uncoupling Hepatic Oxidative Phosphorylation Reduces Tumor Growth in Two Murine Models of Colon Cancer
Rachel J. Perry,^{1,2,3} Dongyan Zhang,¹ Xian-Man Zhang,³ James L. Boyer,^{1,4} & Gerald I. Shulman^{1,2,4*}

Controlled-release mitochondrial protonophore reverses diabetes and steatohepatitis in rats
Rachel J. Perry,^{1,2,3} Dongyan Zhang,¹ Xian-Man Zhang,³ James L. Boyer,^{1,4} & Gerald I. Shulman^{1,2,4*}

Outstanding Collaborations

Article **Cell**

Origin and Function of Stress-Induced IL-6 in Murine Models
Hua Qing,^{1,2} Reine Desrosneaux,^{1,2,3} Kavita Irani-Winger,¹ Yann S. Mineur,¹ Nia Fogelman,¹ Cullin Zhang,^{1,2} Sarah Rashed,¹ Noah W. Palm,¹ Rajita Sinha,¹ Marina B. Piccolotto,¹ Rachel J. Perry,¹ and Andrew Wang^{1,2,3*}

Dehydration and insulinopenia are necessary and sufficient for euglycemic ketoacidosis in SGLT2 inhibitor-treated rats
Rachel J. Perry,^{1,2} Aviva Rabin-Cour,¹ Jeongyu D. Song,¹ Rebecca L. Cardone,¹ Yongliang Wang,¹ Richard G. Kibbey,^{1,2} & Gerald I. Shulman^{1,2*}

Research Attracted Pharma Collaborations/Awards

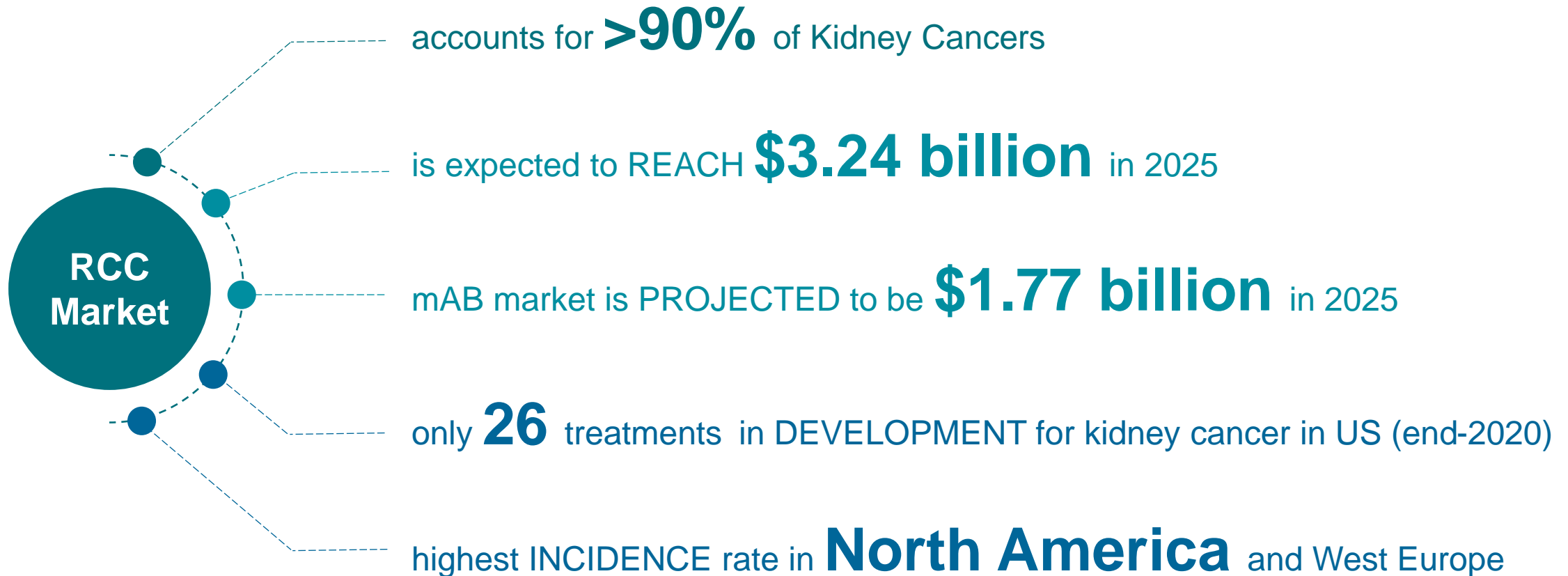
AstraZeneca

GILEAD
THE LIVER COMPANY, INC.

Blavatnik Awards Young Scientists

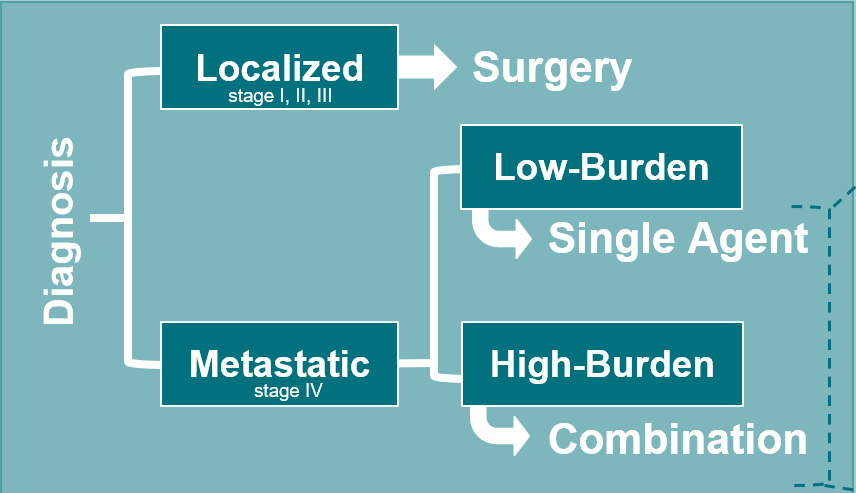
Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

The Global Market for Renal Cell Carcinoma



Renal Cell Carcinoma patients lack effective therapies

Standard Of Care



*Many RCCs are clinically silent with diagnosis in stage IV

MOA	Drug	Company
mTORi	Everolimus	Brand: Novartis Generic: Multiple
TKRi VEGFR1-3i	Sunitinib	Brand: Accord Healthcare S.L.U. Generic: Sun Pharmaceutical Industries Inc.
	Lenvatinib	Eisai Inc.
+	PD-1i	Pembrolizumab Merck

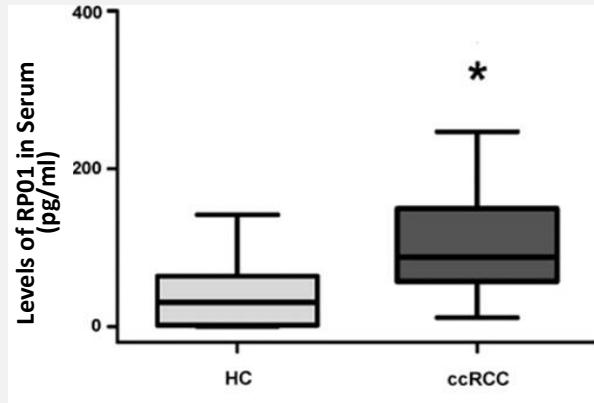
Current therapies have **side effects** and frequent **resistance**,
with **limited efficacy**.

We aim to develop the first RP01 neutralizing antibody for the treatment of renal cell carcinoma

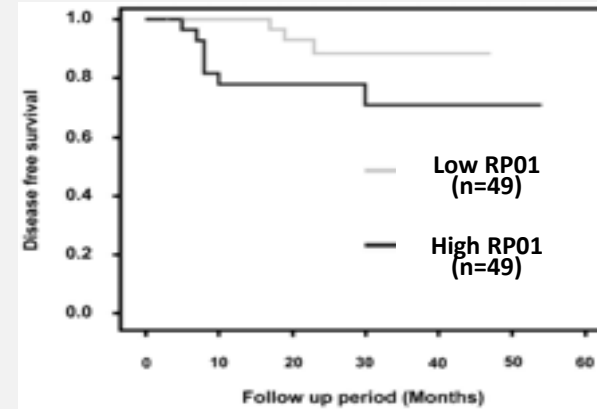
RP01 is increased in RCC patients and cause tumors in mice



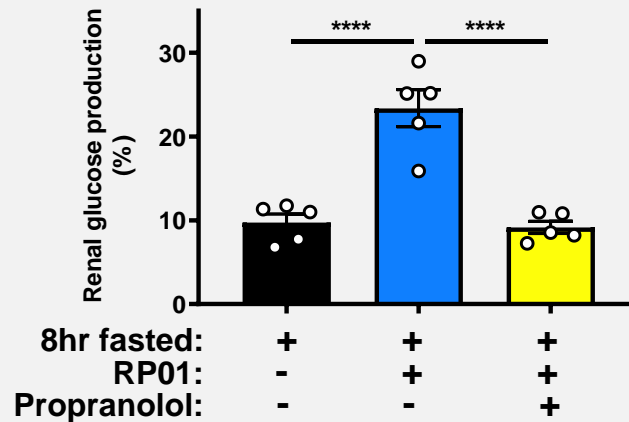
RP01 is increased in RCC patients



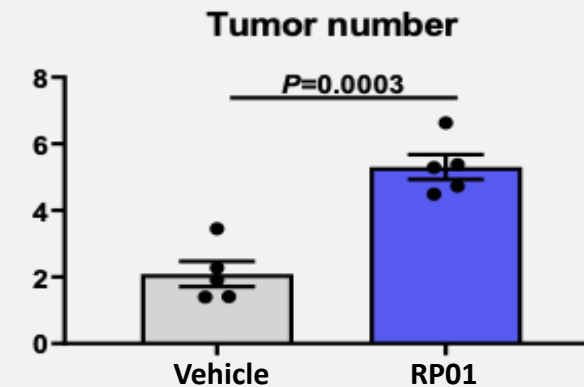
High RP01 is associated with worse survival



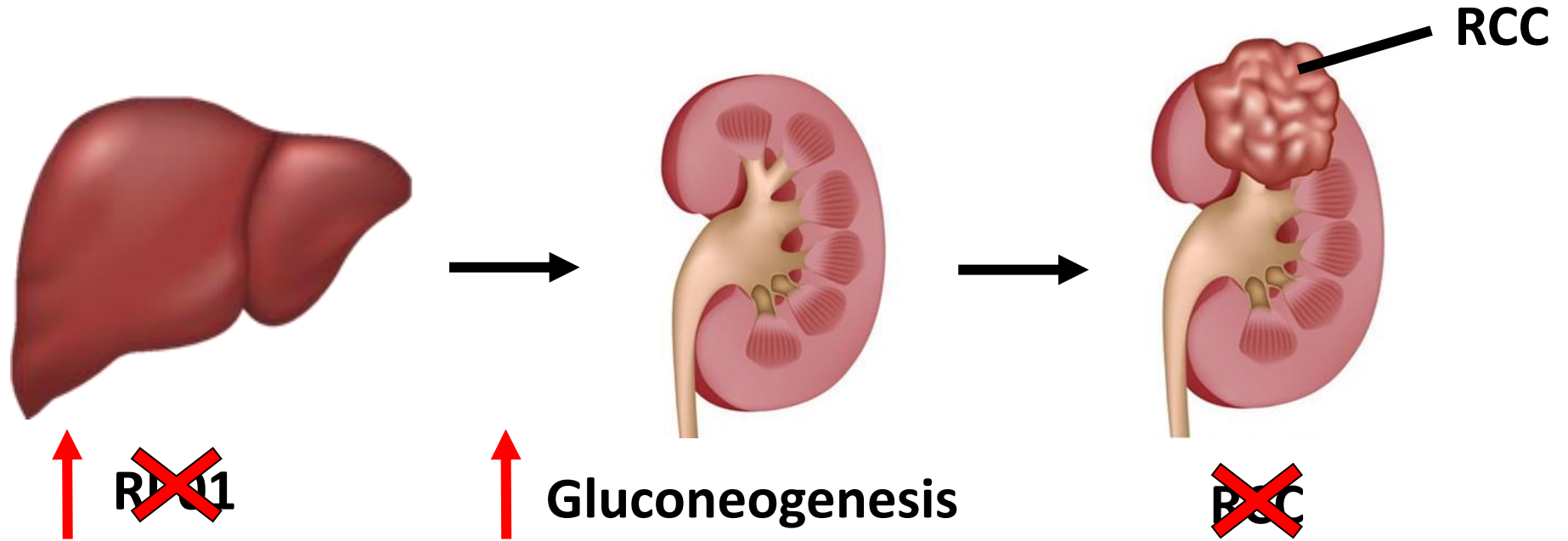
RP01 increases renal gluconeogenesis



Increased RP01 cause RCC tumors in mice



The development of an RP01 neutralizing antibody is key for a solid POC



We have a clear GO / NO GO strategy

Future Plans with Blavatnik Fund

	Stage I	Stage II	Stage III	
Goal	Develop RP01 neutralizing antibody (RP01 ab)	Test if RP01ab Reduces renal gluconeogenesis	Evaluate RP01ab's efficacy against RCC mouse models	
Method	External CRO	Fasting/diabetic mouse models	Xenograft tumor studies w/ RP01-high RCC human cell lines	Spontaneous RCC mouse models
Funding Timeline	\$60K 6 months		\$240K 6 months	
			Long-Term Proof of Concept	

Longer Term Plan:
We aim to form a metabolic oncology NewCo from this and other projects with related programs from Yale Collaborators

RP01 blocking antibody has NO direct competitors

- There are **NO** THERAPEUTIC **blocking antibodies** for RP01 developed or in development
- **Approved** DRUGS for RCC have **limited efficacy** in ADVANCED DISEASE
- Increased circulating RP01 is IMPLICATED in **other diseases**
 - Future Market Opportunities:
 - Muscle-manifesting mitochondrial disorders
 - Chronic hyperinsulinemia, obesity, insulin resistance, T2D
 - Coronary heart disease

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Thank You!

We would like to thank the Blavatnik associates for their help:

Qi Want

Jonathan Dow

Sarah Dudgeon