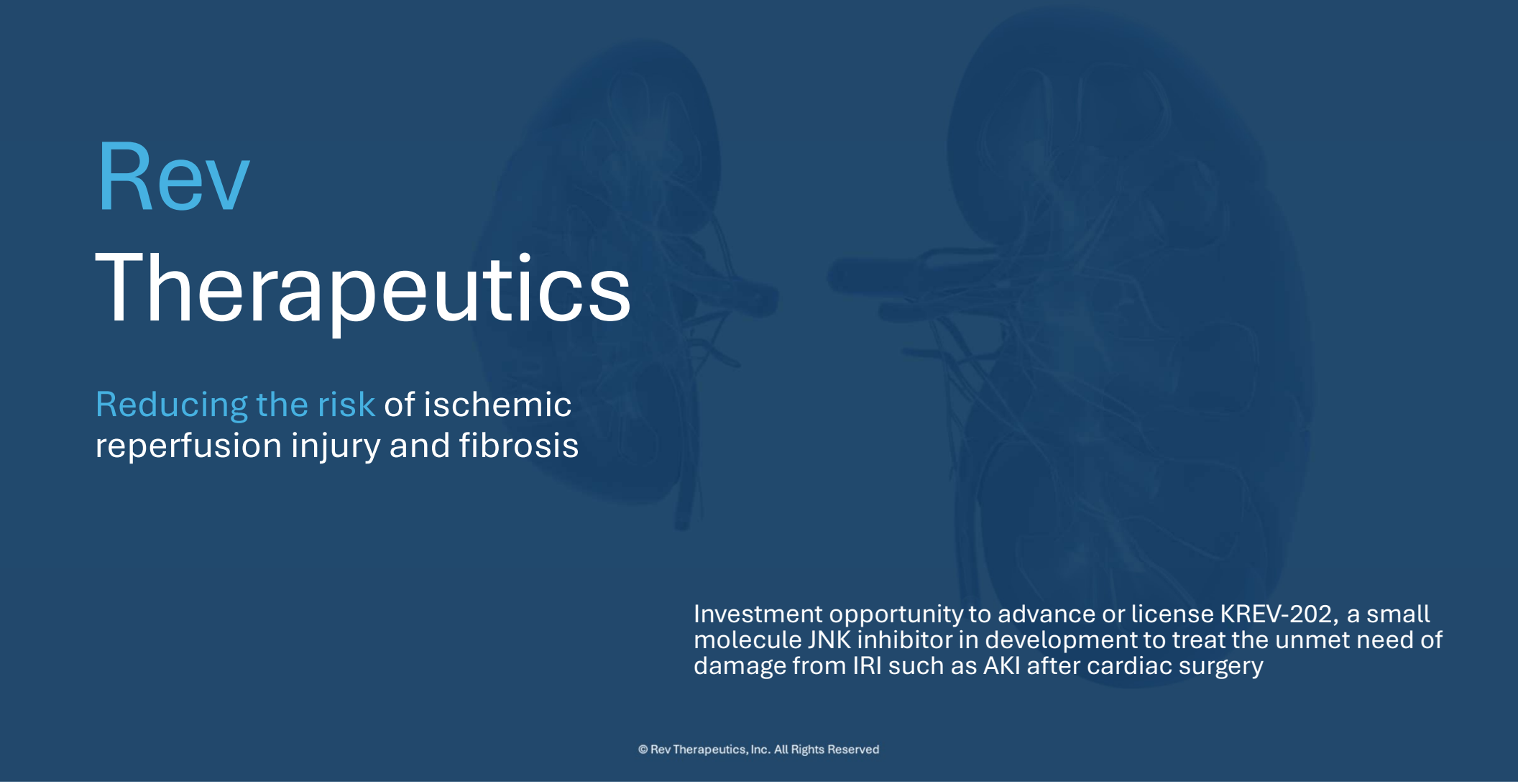
Rev Therapeutics

Reducing the risk of ischemic reperfusion injury and fibrosis



Investment opportunity to advance or license KREV-202, a small molecule JNK inhibitor in development to treat the unmet need of damage from IRI such as AKI after cardiac surgery

Experienced team with extensive development and clinical experience

Business Development, Finance, Operations		Clinical and Reg. Affairs	Nonclinical Development and Toxicology		CMC and Operations
					
David Webb, Ph.D. Chairman Former VP of Research, Celgene Synbal, Agragene, Syrrx, Cadus, OSI Pharma, Syntex, Roche LinkedIn	**Derek R. Brunelle** CFO Former Executive Director, J.P. Morgan Managing Director, Silicon Valley Bank LinkedIn	**Elizabeth Squiers, M.D.** CMO, acting CEO Former CMO at Quark Pharmaceuticals, Genani, and Y's Therapeutics LinkedIn	**Rick Morrissey, Ph.D.** SVP Development Former VP of Development, Celgene Schering Plough, Merck LinkedIn	**Sanjeev Thohan, Ph.D.** VP Nonclinical Development* Former VP Nonclinical Development, Kinnate Biopharma, Snr. Director, Preclinical Safety, Xeris, Novartis LinkedIn	**Yoshi Satoh, Ph.D.** CSO Former medicinal chemist, 5 clinical compounds at Novartis and Celgene LinkedIn

Co-developed FDA-approved products include: Erlotinib (Tarceva®), Alogliptin (Nesina®), Apremilast (Otezla®), Temozolomiode (Temodal®), Anti-thymocyte Globulin (Thymoglobulin®), Mycophenolate mofetil (CellCept®), Cyclosporine (SangCYA®), Celsior® (510k device), Cysteamine bitartrate (PROCYSBI®), Pomalidomide (Pomalyst®), Ezetimibe (Zetia®), Rifaximin (Xifaxan ®), Cabozantinib (Cabometyx®), Cobimetinib (Cotellic®), Tafenoquine, Asciminib (Scemblix®), Tecovirimat, Gvoke

* Consultant

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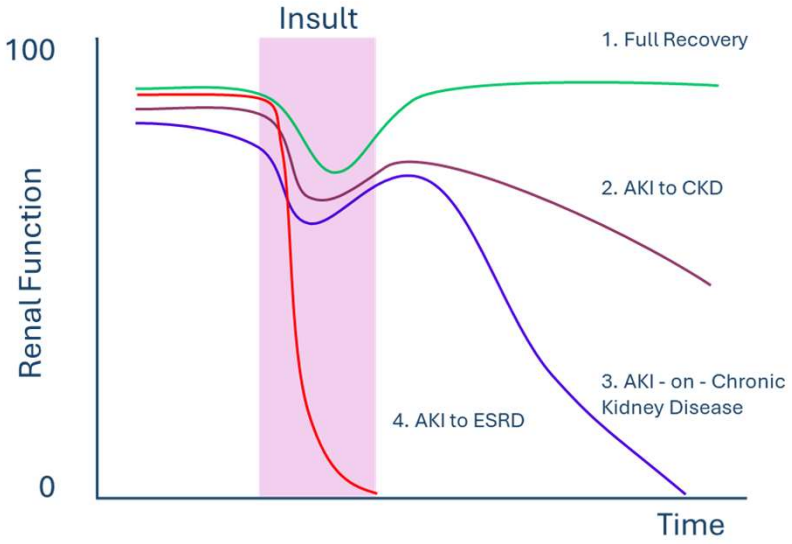
Opportunity summary

Large $1B - $2B market	We are currently developing KREV-202, a patent protected [1] prodrug of CC-930 (tanzisertib)[2] to prophylactically treat ischemic reperfusion injury and resultant fibrosis such as follows cardiac surgery-associated acute kidney injury (CSA – AKI), a large unmet medical need
De-risked asset	CC-930 was tested in multiple clinical studies, including a 56-week Ph. 2 study treating patients with IPF (NCT 01203943) and was well tolerated during the initial 4-week double blind ascending dose phase with largely no reduction in FVC through 32 weeks, in contrast to reduction seen with some approved IPF drugs[3]
Compelling preclinical data	Preclinical *in-vivo* animal data using KREV-202 corroborates the mitigation of repurfusion injury and fibrosis of CC-930 shown in prior kidney ischemia / reperfusion injury animal preclinical models
Experienced team	Capital efficient virtual business model supported by team members with decades of drug development and renal disease experience; team members co-developed 17 approved drugs and collaborated on 100+ IND filings

[1] US national phase application filed; EU national phase filed
[2] JNK inhibitor developed by Celgene that is no longer being developed based on confirmation from BMS (acquired Celgene in 2019)
[3] van der Velden et al., (2016), JNK inhibition reduces lung remodeling and pulmonary fibrotic systemic markers. Clin Trans Med, 5: e36. https://doi.org/10.1186/s40169-016-0117-2

IV treatment of acute indication and unmet need

One example of the unmet need of IRI and resultant fibrosis is Cardiac surgery-associated acute kidney injury (CSA-AKI) is a common complication of coronary artery bypass graft (CABG) surgery which can progress to chronic kidney disease and end stage renal disease



270,000+

Est. # of CABG procedures performed annually in U.S.

10% - 30%

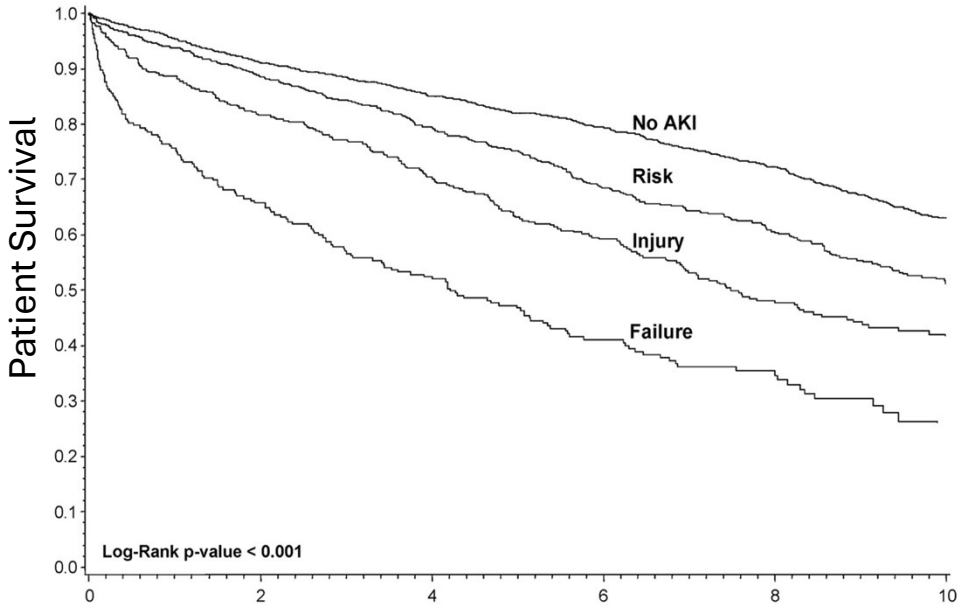
Incidence rate of CSA-AKI per CABG procedure

2% - 5%

Patients diagnosed with CSA- AKI require renal replacement therapy

The impact on lives and healthcare system costs

CSA-AKI is associated with poorer outcomes for patients as well as increased costs for healthcare payors



Increased Mortality

Post CABG survival rates are significantly impacted by severity of AKI diagnosis

2x Cost

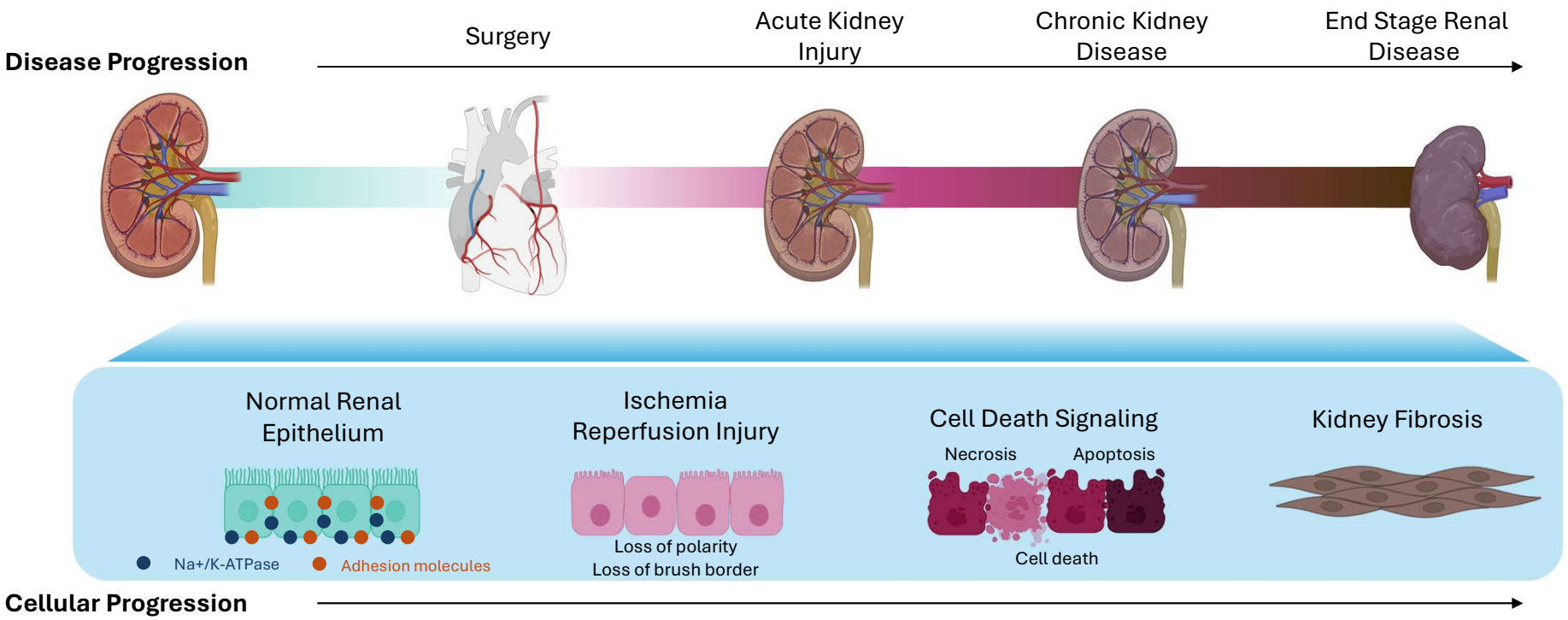
Index hospitalization costs for those with AKI ($77.1k vs. $38.8k)

$1.0B

Est. total incremental hospitalization costs associated with incidence of AKI

The underlying cause of the problem

Ischemia and reperfusion injury progresses to renal proximal tubular epithelial (RPTE) cell death, kidney dysfunction, and fibrosis



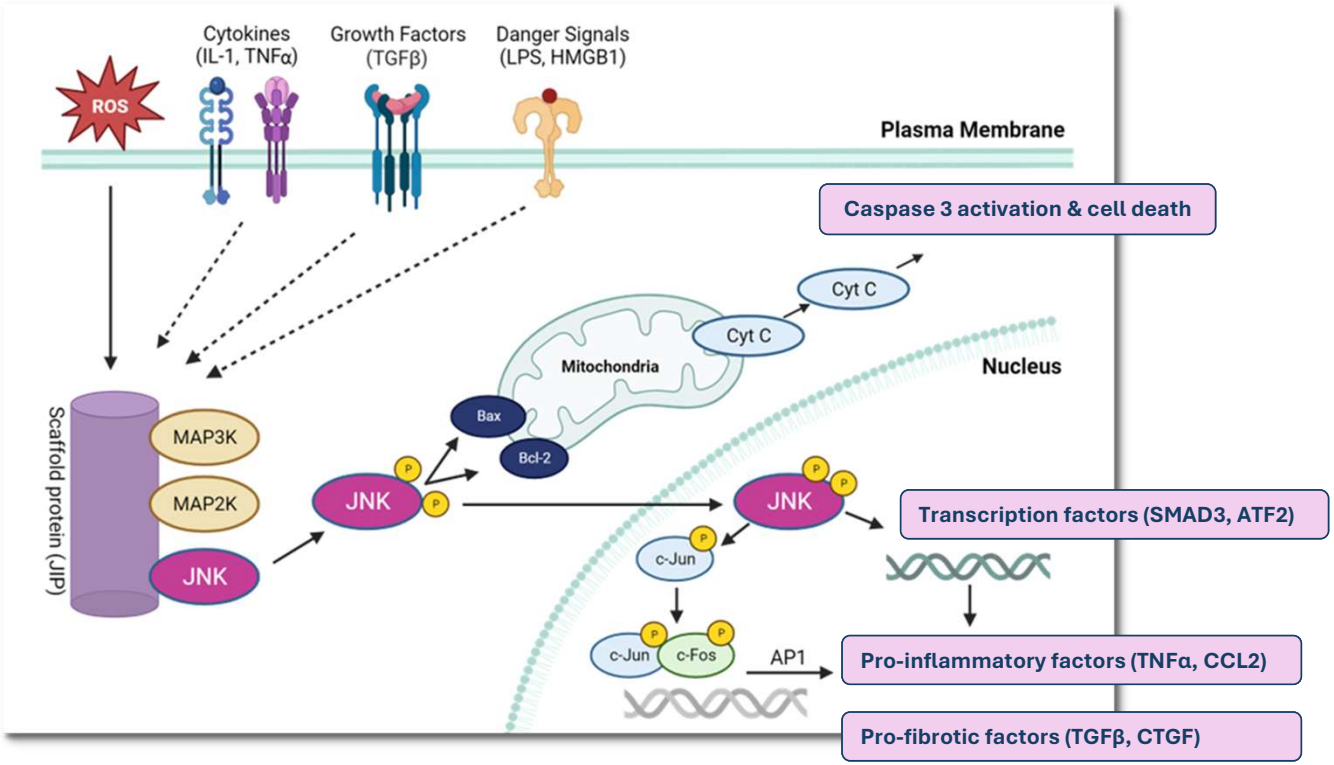
KREV-202 Program

JNK pathway is associated with cell death, damage, and fibrosis

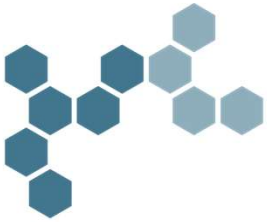
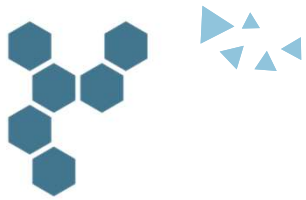
JNK enzymatic pathway is activated in response to various cellular stresses and plays an important role in cell death and inflammation

Activation of the JNK pathway is a common feature in human kidney injury

JNK inhibition can impact inflammation, cell death, and fibrosis



KREV-202 –a novel prodrug compound with unique properties extends use to IV administration

Parent Compound	Prodrug Compound	*In-vivo* Compound
Chemical Modification →		*Enzymatic Cleavage*
CC-930	KREV-202	CC-930
		
Active moiety		*Active moiety*
✓ Efficacy in multiple animal models	✓ Water soluble | allows IV admin	✓ Efficacy in animal models
✓ Shown to be safe in humans	✓ Rapidly cleaves to active moiety	✓ Anticipated to be safe in humans
✓ Selective for primary target	✓ Prodrug moiety has no activity	
✗ Insoluble, orally available	✓ Prodrug group used in approved drugs	

KREV-202 is rapidly cleaved to the active species (CC-930) by isoforms of alkaline phosphatase which are widely distributed throughout mammalian tissues

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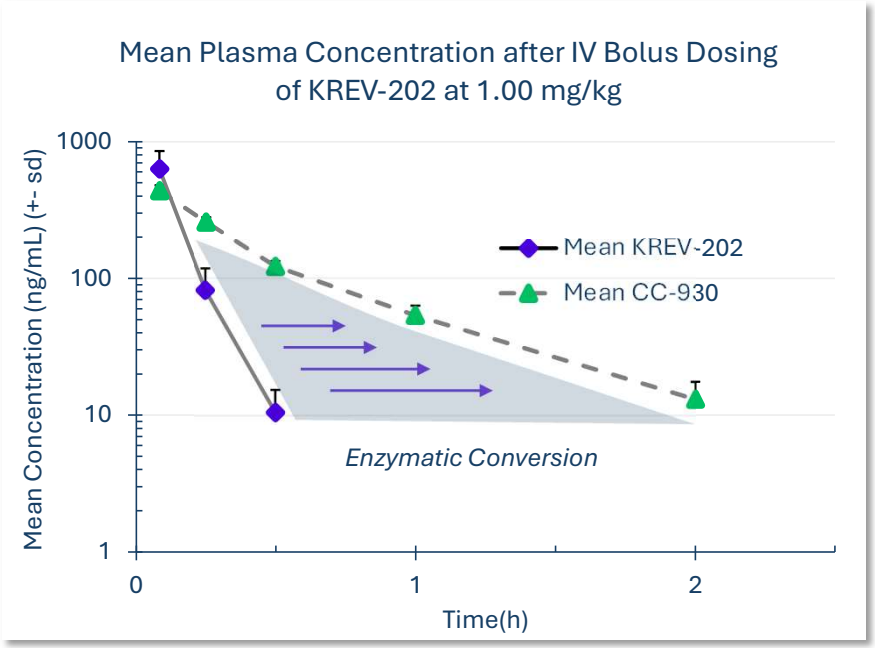
Rapid enzymatic cleavage to facilitate IV administration

KREV-202 shows superior pharmaceutical properties and is rapidly cleaved to CC-930 *in-vivo* (1)



Solubility Comparison

Compound	Solubility in PBS* at pH 7.4
KREV-202	45.6 mg/ml
CC-930	0.060 mg/ml

1. Rev Therapeutics Data on file

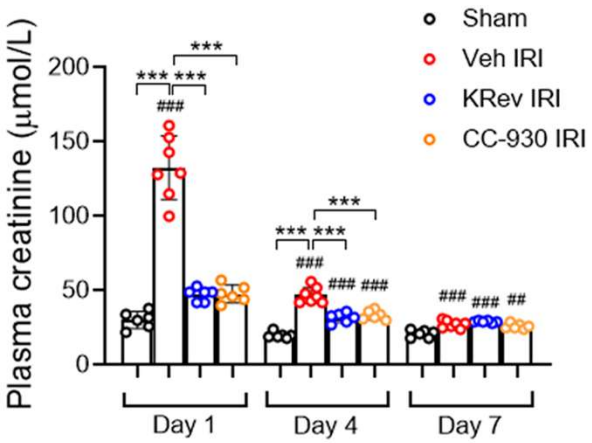
Why we are excited about KREV-202

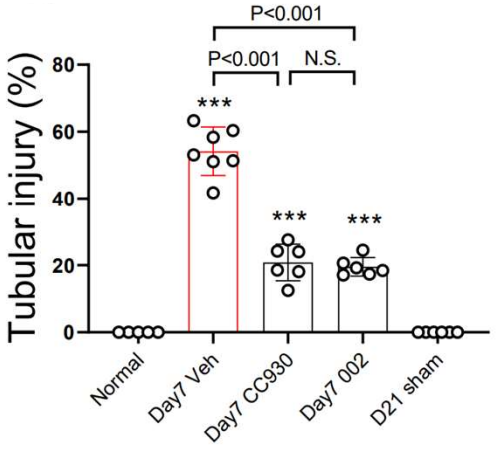
In *in-vivo* animal studies[1], KREV-202 showed a significant ability to protect against renal failure, renal inflammation, and renal fibrosis

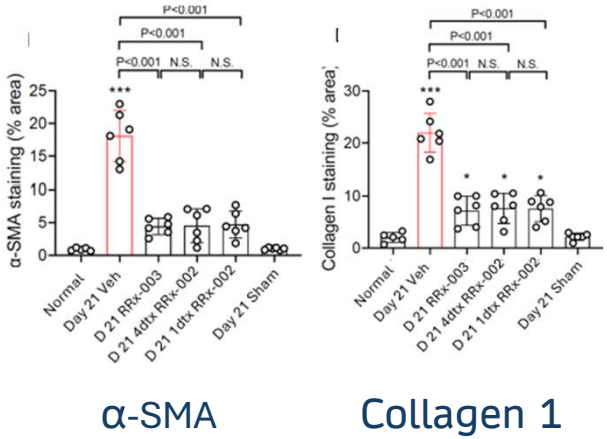
88% Reduction in plasma creatinine

65% Reduction in tubular damage

79% Reduction in fibrosis markers







α-SMA Collagen 1

Note: RRx-003 is internal name for CC-930 ; RRx-002 was original compound name of KREV-202

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1. Nikolic-Paterson DJ et al, 2026 https://doi.org/10.3389/fphar.2025.1667221

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Appendix

Competitive landscape

Known agents currently in development

Sponsor	Stage	Agent	Modality	MoA	NCT	Primary Endpoint
Novartis	Ph. 2	TIN816	Recombinant human CD39 enzyme	ATP Modulator	NCT05524051	Ratio of highest serum creatine value within 5 days post-dose vs. baseline
Astra Zeneca	Ph. 3	Ultomiris™	mAb	C5 inhibitor	NCT05746559	No. of participants experiencing major adverse kidney events (MAKE) at 90 days post CPB surgery
Renibus Therapeutics	Ph. 3	RBT-1	Combo of stannic protoporphyrin & iron sucrose	Preconditioning agent	NCT06021457	Composite of death, incidence of AKI requiring RRT, ICU days, and 30-day cardiopulmonary
AM Pharma	Ph. 2	Ilofotase alfa	Recombinant alkaline phosphatase (recAP)	Dephosphorylating and detoxifying DAMPs and PAMPS	Not available	01/16/2024 press release – "ratio between pre-and post-surgery creatine levels"
Guard Therapeutics	Ph. 2b	RMC-035	Recombinant protein (mimic of alpha-1 microglobulin)	Reductase activity, binding of free radicals and heme, and binding, protection of mitochondria	Not available	01/30/2024 R&D Day – "Change from baseline in eGFR based on serum creatine at Day 90"
Revelation Bio Sciences	Ph 1	Gemini	Toll 4 agonist	Anti-inflammatory	NCT06863467	Safety Tolerability, Cytokine levels in CKD 3/4 patients

Select scientific papers about CC-930

Title	DOI
Plantevin Krenitsky V, Nadolny L, Delgado M, et al. Discovery of CC-930, an orally active anti-fibrotic JNK inhibitor. Bioorganic & Medicinal Chemistry Letters. 2012 Feb;22(3):1433-1438.	DOI: 10.1016/j.bmcl.2011.12.027
van der Velden, J.L.J., et al. (2016), JNK inhibition reduces lung remodeling and pulmonary fibrotic systemic markers. Clin Trans Med, 5: e36.	DOI 10.1186/s40169-016-0117-2
Grynberg Keren, Ma Frank Y. , Nikolic-Paterson David J., The JNK Signaling Pathway in Renal Fibrosis. Frontiers in Physiology, vol. 8 (2017)	DOI=10.3389/fphys.2017.00829
Keren Grynberg, et al., JUN Amino-Terminal Kinase 1 Signaling in the Proximal Tubule Causes Cell Death and Acute Renal Failure in Rat and Mouse Models of Renal Ischemia/Reperfusion Injury, The American Journal of Pathology, Volume 191, Issue 5, 2021, Pages 817-828,	https://doi.org/10.1016/j.ajpath.2021.02.004

Select scientific papers about CSA-AKI

Title	DOI
Vives M, Hernandez A, Parramon F, Estanyol N, Pardina B, Muñoz A, Alvarez P, Hernandez C. Acute kidney injury after cardiac surgery: prevalence, impact and management challenges. Int J Nephrol Renovasc Dis. 2019 Jul 2;12:153-166.	10.2147/IJNRD.S167477
Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med. 1998 Apr;104(4):343-8.	10.1016/s0002-9343(98)00058-8
Bonventre, J.V. and Yang, L., 2011 Cellular pathophysiology of ischemic acute kidney injury. *J Clin Invest*. 2011;121(11):4210-4221.	10.1172/JCI45161
Alshaikh HN, Katz NM, Gani F, Nagarajan N, Canner JK, Kacker S, Najjar PA, Higgins RS, Schneider EB. Financial Impact of Acute Kidney Injury After Cardiac Operations in the United States. Ann Thorac Surg. 2018 Feb;105(2):469-475.	10.1016/j.athoracsur.2017.10.053
Schurle A, Koyner JL. CSA-AKI: Incidence, Epidemiology, Clinical Outcomes, and Economic Impact. J Clin Med. 2021 Dec 8;10(24):5746.	10.3390/jcm10245746
Casanova, A.G.; Sancho-Martínez, S.M.; Vicente-Vicente, L.; Ruiz Bueno, P.; Jorge-Monjas, P.; Tamayo, E.; Morales, A.I.; López-Hernández, F.J. Diagnosis of Cardiac Surgery-Associated Acute Kidney Injury: State of the Art and Perspectives. *J. Clin. Med.* 2022, *11*, 4576.	10.3390/jcm11154576
Leaf DE, Waikar SS. End Points for Clinical Trials in Acute Kidney Injury. Am J Kidney Dis. 2017 Jan;69(1):108-116.	10.1053/j.ajkd.2016.05.033

Contact information

Thank you!

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