GUARD THERAPEUTICS

Targeted therapies for kidney diseases

Non-confidential summary

April 2024

GUARD THERAPEUTICS – IN SHORT

- Clinical stage biotechnology company focusing on kidney diseases
- Lead investigational drug RMC-035 developed for prevention & treatment of kidney injury in relation to open heart surgery
  - Granted Fast Track Designation by the FDA
- Recently completed Phase 2 study (n=177) demonstrated robust efficacy on clinically relevant kidney endpoints (eGFR, MAKE)
- Entering Phase 2b dose-finding study (POINTER) followed by a single Phase 3 study with potential for conditional (accelerated) approval
- Lead indication USD >1 bn opportunity alone – no approved therapies
- Preclinical peptide platform based on RMC-035 mechanism with strong efficacy in CKD models, addressing even larger market opportunities
- Listed on Nasdaq First North Growth Market in Stockholm [GUARD]

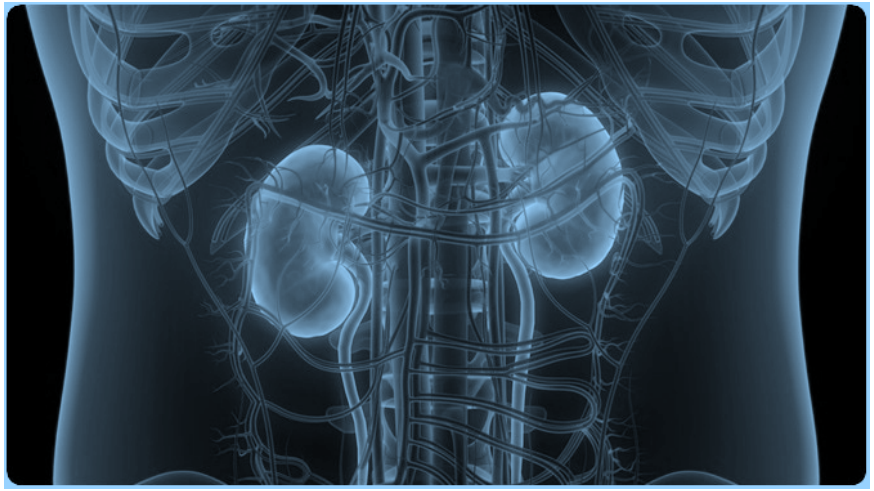
eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney events; CKD, chronic kidney disease

EXPERIENCED MANAGEMENT TEAM WITH PROVEN TRACK RECORD IN GLOBAL DRUG DEVELOPMENT

NAME / POSITION	EXPERIENCE		NAME / POSITION	EXPERIENCE	
 **TOBIAS L. AGERVALD** MD, PhD, CEO	**+10** years in industry	astellas	 **KARIN BOTHA** MSc, CFO	**+20** years in industry	NOVARTIS SmithKline Beecham gsk GlaxoSmithKline
 **MICHAEL REUSCH** MD, CMO	**+30** years in industry	Fujisawa astellas	 **PETER GILMOUR** MSc, PhD, CSO/Head of Preclinical	**+20** years in industry	AstraZeneca astellas
 **TORBJÖRN LARSSON** BSc, Head of CMC	**+30** years in industry	Medivir aprea therapeutics Pharmacia & Upjohn	 **SARA THURESSON** MSc, Head of Clinical Operations	**+15** years in industry	oncopeptides WILSON THERAPEUTICS IQVIA Medivir

KIDNEY DISEASE – A SIGNIFICANT UNMET MEDICAL NEED

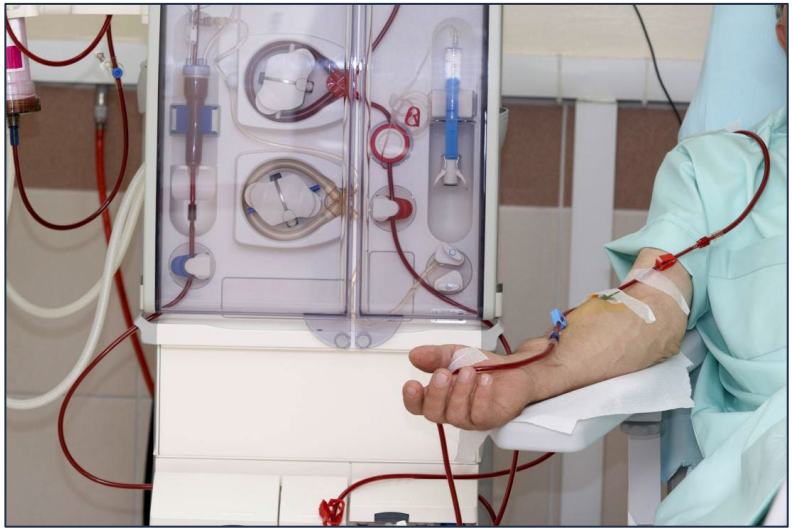
Acute injury → Chronic kidney disease (eg, diabetes, high blood pressure) → End-stage kidney disease (ESKD)



ESKD, end-stage kidney disease

END-STAGE KIDNEY DISEASE – A DEVASTATING CONDITION WITH POOR OUTCOME

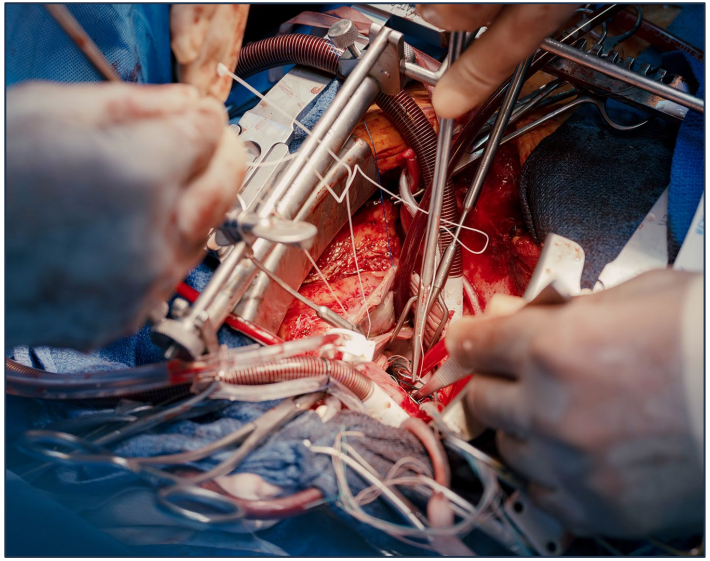
- Requires life-long dialysis treatment (or kidney transplantation)
- Annual mortality remains unacceptably high (15-20%)
- Prognosis worse than many forms of metastatic cancer
- Cost of patient management very high – prevention is cost-effective



P Stenvinkel and TE Larsson, Am J Kidney Dis, 2013 Aug;62(2):339-51

KIDNEY INJURY IN OPEN HEART SURGERY

- Nearly half a million Coronary Artery Bypass Graft (CABG) and/or valve replacement surgeries performed each year (US/Europe)
- Procedure often causes substantial kidney injury (collateral damage)
- Kidney injury frequently becomes permanent
  - Incident chronic kidney disease (CKD)
  - Progressive CKD & End-Stage Kidney Disease (ESKD)
  - Associated comorbidities, eg cardiovascular disease



No approved drugs to prevent or treat kidney injury in this setting

CABG, coronary artery bypass graft; CKD, chronic kidney disease; ESKD, end-stage kidney disease

Meersch et al. Intensive Care Med (2017); Mozaffarian et al. Circulation (2016); OECD/EU Health at a glance (2016); 2. Pickering JW et al. Acute kidney injury and prognosis after cardiopulmonary bypass: a meta-analysis of cohort studies, Am J Kidney Dis. 2015 Feb; Epidemiology data on file

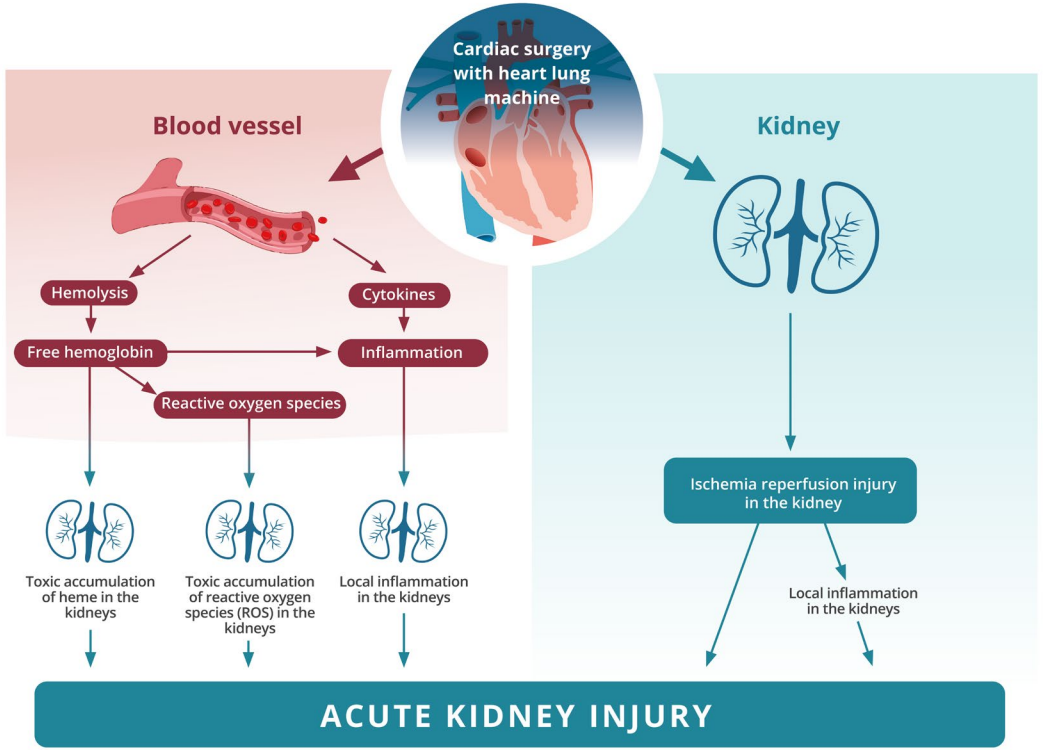
MECHANISMS OF KIDNEY INJURY IN OPEN HEART SURGERY

Two key contributing factors:

- Ischemia-reperfusion injury (IRI)
- heme toxicity (hemolysis)

Secondary events:

- Mitochondrial dysfunction
- Inflammatory response



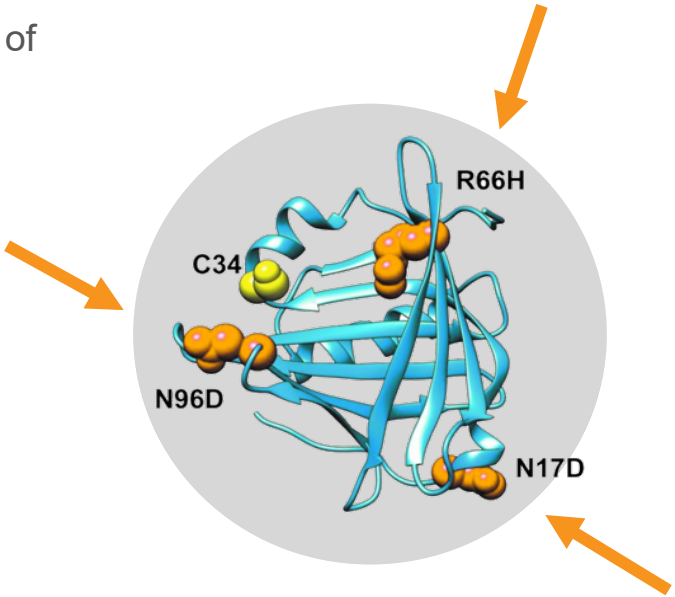
IRI, ischemia-reperfusion injury

Wang et al, Nat Rev Nephrol 2017; Bonventre et al, J Clin Invest 2011

Our product – RMC-035

RMC-035 IS FIRST-IN-CLASS WITH CLINICALLY VALIDATED MECHANISM

- RMC-035 is a druggable, recombinant & patent protected variant of endogenous protein alpha-1-microglobulin (A1M)
- Administered by IV infusion
- Improved physicochemical properties compared to native A1M:
  - Three amino acid substitutions to improve solubility
  - N-terminal tag for increased stability & solubility
  - Lack of glycosylation (manufactured in E. coli)

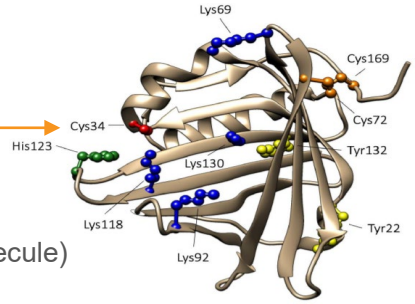


Provides a druggable protein with favorable drug properties

A1M, alpha-1-microglobulin; E coli, Escherichia coli

A1M STRUCTURE & FUNCTION ARE WELL CHARACTERIZED

- Amino acid residue Cysteine 34 & tertiary protein structure provide the basis for A1M function



Neutralize oxidative stress

- **Reductase activity** (reduction of 5-6 free radicals per A1M molecule)
- **Free radical trapping** (covalent trapping of 3-4 radicals per A1M molecule)

Clean up free heme

- **Heme binding & degradation** (two specific heme-binding sites, binds heme in a 2:1 molar ratio)

Protect from mitochondrial stress

- **Mitochondrial binding/stabilization** (binding to Cytochrome C, Complex I)

A1M, alpha-1-microglobulin

RMC-035 – A NOVEL PARADIGM FOR KIDNEY PROTECTION

Evolutionary conserved mechanism
– aligned with pathophysiology of acute kidney injury

Robust preclinical efficacy in numerous disease models & species
– provides translational confidence

Preferential biodistribution to kidney (tubular cells)
– main site of cellular injury in open-heart surgery

Clinical Phase 2 (AKITA) data with 177 patients
– clinically meaningful kidney protection

First therapy in open-heart surgery with consistent efficacy on clinically relevant kidney outcomes (eGFR, MAKE)

eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney events

Clinical data with RMC-035

PHASE 1 DATA – RMC-035 IS SAFE & WELL TOLERATED

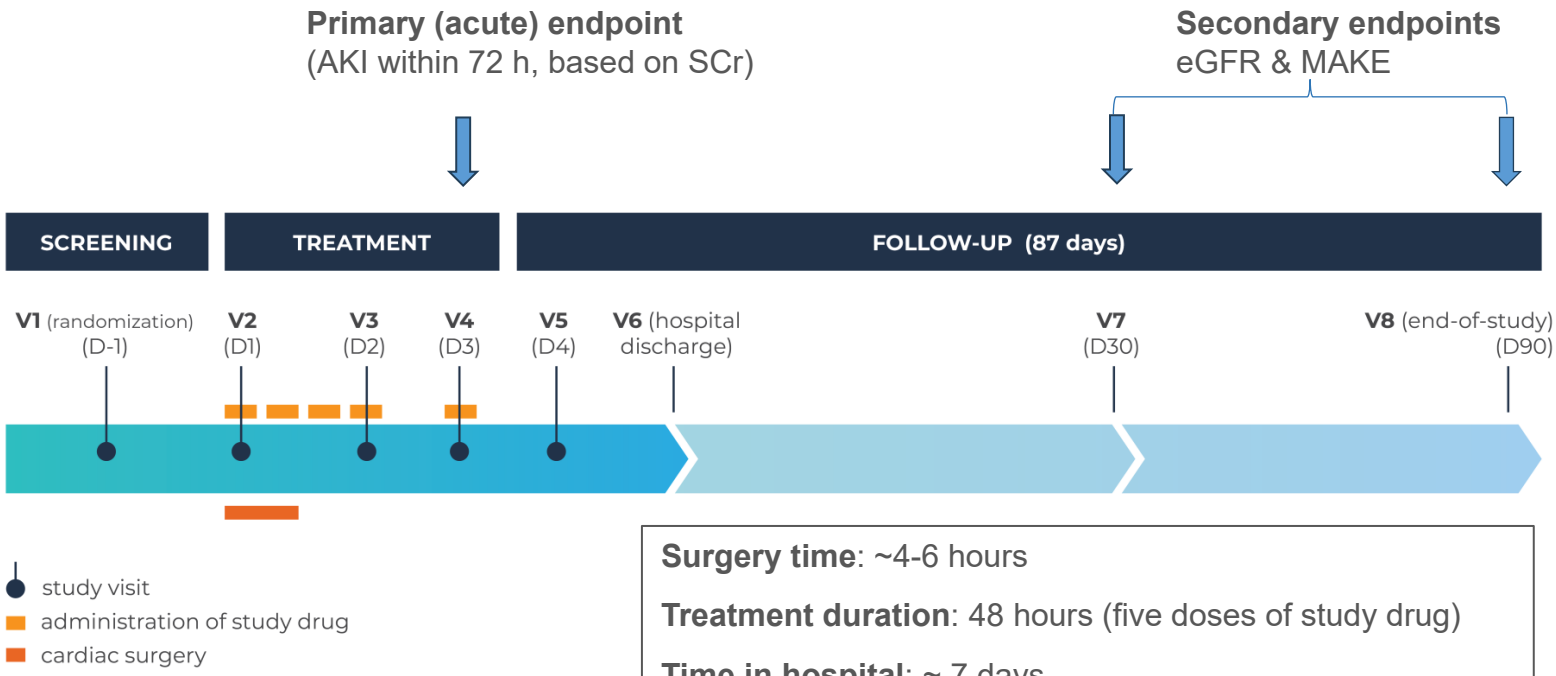
- 52 subjects exposed to RMC-035 in four Phase 1 studies
- No serious adverse events (SAEs) related to study drug
- Pharmacokinetic profile consistent with small therapeutic protein (short half-life due to renal clearance)

Study	Phase	Population	Dosing	Key objectives	Locations	Status
ROS-01	Phase 1	Healthy subjects	Single dose (0.08-2.6 mg/kg)	Safety, tolerability	Sweden	Completed
ROS-02	Phase 1	Healthy subjects	Multiple dosing (0.43-1.3 mg/kg)	Safety, tolerability	Sweden	Completed
ROS-03	Phase 1	Renal impairment	Single dose (0.22 or 0.43 mg/kg)	Pharmacokinetics	Sweden	Completed
ROS-04	Phase 1b	Cardiac surgery	Multiple dosing (0.65 or 1.3 mg/kg)	Safety, tolerability	Germany	Completed

PHASE 2 STUDY (**AKITA**) – MAIN OBJECTIVES

- Randomized, placebo-controlled, adaptive, parallel group study
  - Global study with patient enrolment in EU, Canada, US
- Objective to establish relevant efficacy signal(s) to guide further development
- Multiple endpoints for evaluation:
  - Acute endpoints – short-term prognostic markers for clinically relevant long-term outcomes
  - Chronic endpoints – clinically relevant kidney outcomes to be confirmed in Phase 3 (to support marketing approval)
- No single Phase 2 endpoint captures all relevant treatment effects

PHASE 2 AKITA STUDY – OVERVIEW & FLOWCHART



Surgery time: ~4-6 hours

Treatment duration: 48 hours (five doses of study drug)

Time in hospital: ~ 7 days

Follow-up time: up to 90 days after surgery

AKI, acute kidney injury; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney events

SUMMARY OF EFFICACY – PRIMARY & SECONDARY ENDPOINTS

Statistically & clinically significant improvement of kidney function with RMC-035 vs placebo (90 days after surgery)

- Overall net improvement of kidney function (eGFR) > 4 mL/min
  - Efficacy even stronger in CKD patients (6-8 mL/min)
- Reduced proportion of patients with severe loss of kidney function – MAKE90
  - MAKE90 expected primary endpoint in Phase 3
- No efficacy shown based on acute (primary) endpoint, but analyses confounded by a short-lived, reversible increase of SCr with the higher RMC-035 dose
  - Mechanism of SCr increase is well understood – due to tubular overexposure consistent with toxicological evaluations (cynomolgus, marmoset, rodents)
- Efficacy & safety profiles support further development

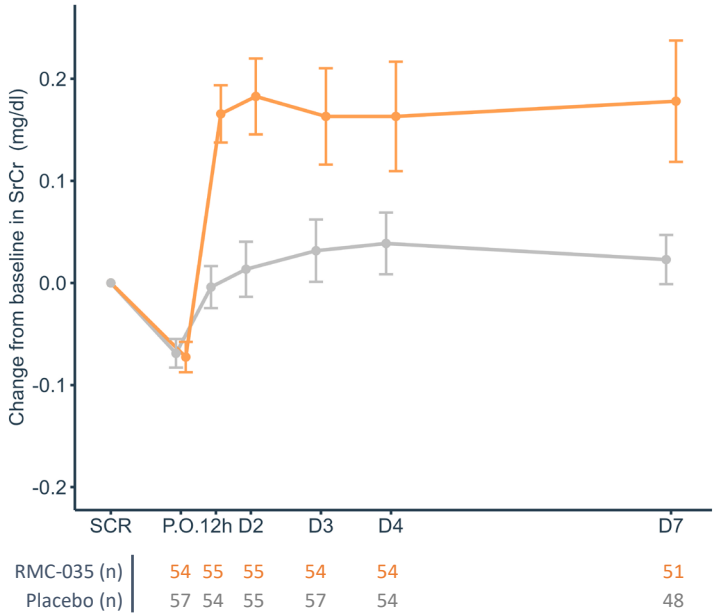
eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; MAKE, major adverse kidney events; SCr, serum creatinine

SERUM CREATININE: CHANGE FROM BASELINE TO DAY 7

ACUTE CREATININE RISE DRIVEN BY HIGHER RMC-035 START DOSE

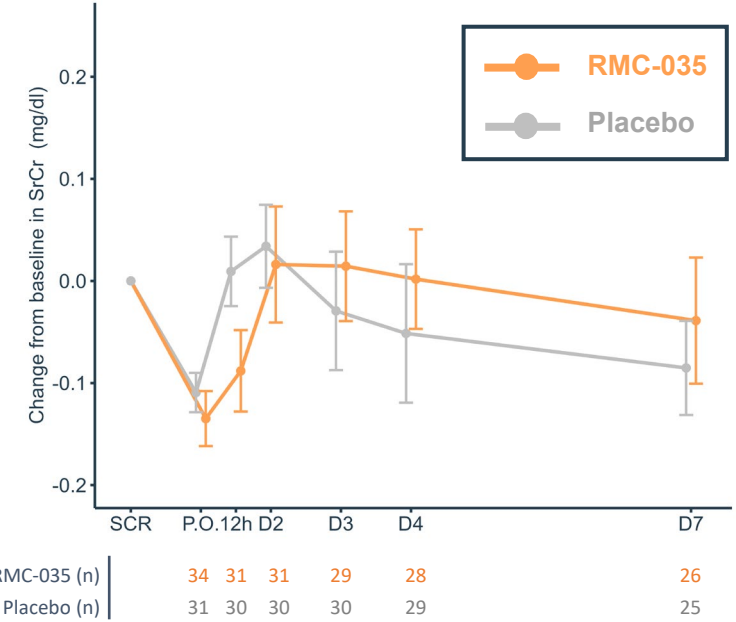
eGFR ≥ 60 mL/min/1.73m^2

Acute SCr increase in patients receiving 1.3 mg/kg RMC-035



eGFR < 60 mL/min/1.73m^2

No SCr increase in patients receiving 0.65 mg/kg RMC-035

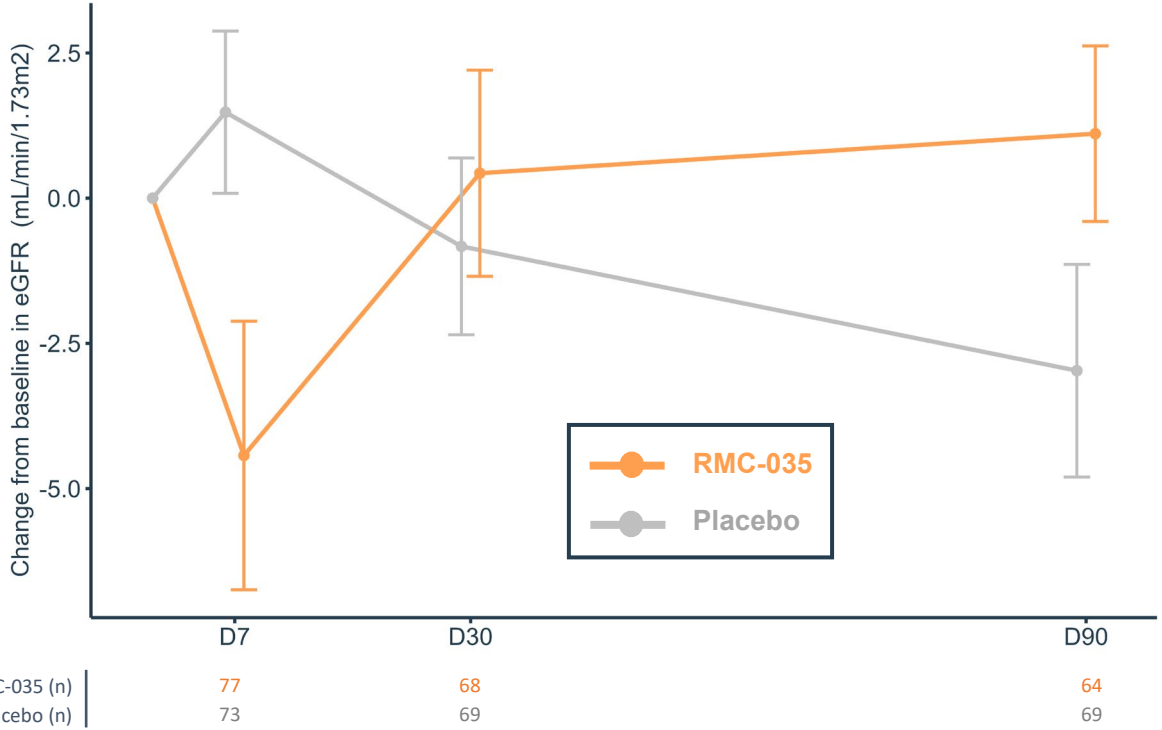


Error bars indicate mean +/- Standard Error (SE); P.O, pre-operative (before surgery); SCR, Screening; eGFR, estimated glomerular filtration rate; SrCr, serum creatinine

Source: Post-hoc analysis of pre-specified endpoint and eGFR subgroup

CHANGE FROM BASELINE IN RENAL FUNCTION (eGFR)

CLINICALLY & STATISTICALLY SIGNIFICANT IMPROVEMENT OF LONG-TERM RENAL FUNCTION WITH RMC-035



eGFR benefit at Day 90:

Measured	MMRM model
4.1 mL/min	4.3 mL/min **p=0.063***

Pre-defined alpha level was 0.1.
P-values < 0.1 are statistically significant.

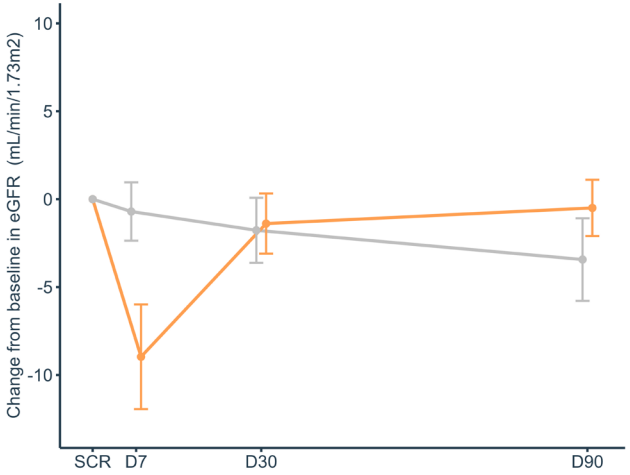
Error bars indicate mean +/- Standard Error (SE); eGFR, estimated glomerular filtration rate; MMRM, Mixed Model of Repeated Measures
Source: Table 14.2.3.3.1.

CHANGE FROM BASELINE IN RENAL FUNCTION (eGFR)

IMPROVEMENT OF LONG-TERM RENAL FUNCTION STRONGER IN SUBGROUP WITH LOWER RMC-035 DOSE (CKD PATIENTS)

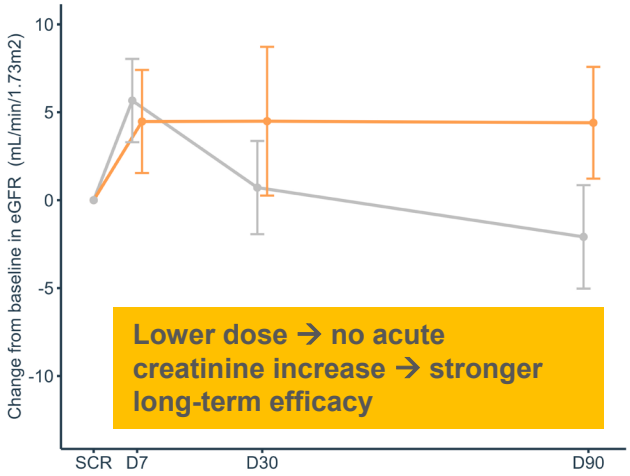
eGFR subgroups pre-specified based on different start doses and risk for kidney injury

eGFR ≥ 60 mL/min/1.73m^2



	SCR	D7	D30	D90
RMC-035 (n)	51	47		43
Placebo (n)	48	43		45

eGFR < 60 mL/min/1.73m^2



	SCR	D7	D30	D90
RMC-035 (n)	26	21		21
Placebo (n)	25	26		24

Lower dose → no acute creatinine increase → stronger long-term efficacy

eGFR benefit at Day 90:

Subgroup	Measured	MMRM model
eGFR ≥ 60	2.9 mL/min	2.3 mL/min p=0.41
eGFR < 60	6.5 mL/min	7.9 mL/min **p=0.051***

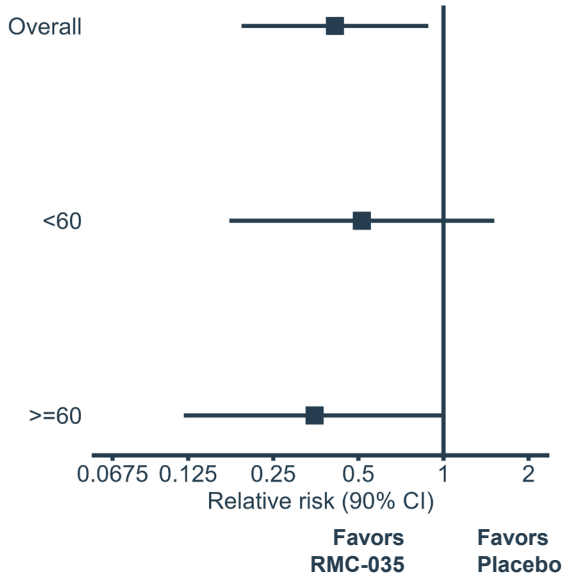
Pre-defined alpha level was 0.1.
P-values < 0.1 are statistically significant.

Source: Table 14.2.3.3.1 Error bars indicate mean +/- Standard Error; MMRM, Mixed Model of Repeated Measures

MAKE90 – REGULATORY PHASE 3 ENDPOINT

CLINICALLY & STATISTICALLY SIGNIFICANT REDUCTION OF MAKE90

	RMC-035 (N=89)	Placebo (N=88)
Number (%) of Subjects with MAKE at Day 90	6 (6.7%)	14 (15.9%)
Death through Day 90	4	4
Dialysis through Day 90	3	2
≥25% eGFR† reduction at Day 90	**3**	**10**
Relative Risk (90% CI)	0.41 (0.19, 0.88) **p=0.047***	



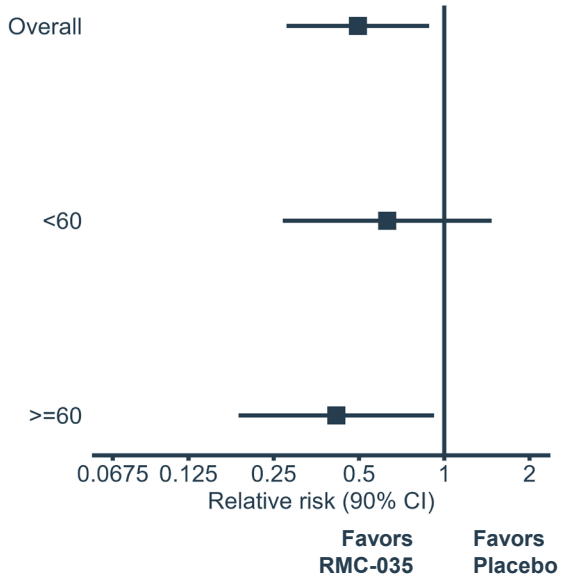
CI, confidence interval
MAKE, Major Adverse Kidney Events, †eGFR calculated using CKD-EPI equation with serum creatinine

Source: Table 14.2.3.9.1

SENSITIVITY ANALYSIS OF MAKE90

CONFIRMS EFFICACY SIGNAL ON REGULATORY PHASE 3 ENDPOINT

	RMC-035 (N=89)	Placebo (N=88)
Number (%) of Subjects with MAKE at Day 90	10 (11.2%)	20 (22.7%)
Death through Day 90	4	4
Dialysis through Day 90	3	2
≥25% eGFR† reduction at Day 90	**7**	**15**
Relative Risk (90% CI)	0.50 (0.28, 0.88) **p=0.041***	

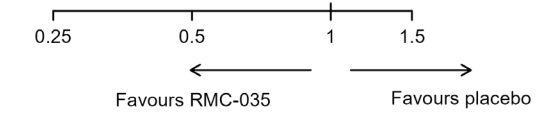


CI, confidence interval
MAKE, Major Adverse Kidney Events, †eGFR calculated using CKD-EPI equation with serum creatinine & cystatin C

Source: Table 14.2.3.9.3

POST-HOC ANALYSIS: RMC-035 CONSISTENTLY REDUCES MAKE90 USING VARIOUS THRESHOLDS OF eGFR LOSS

	RMC-035 Evs/Pts Rate (90% CI)	**Placebo** Evs/Pts Rate (90% CI)	Risk ratio (90 % CI)	p-value
MAKE 90 days (10 % eGFR cutoff)	18/89 20.2 (13.2-27.2)	25/88 28.4 (20.5-36.3)	0.71 (0.46-1.10)	0.200
MAKE 90 days (15 % eGFR cutoff)	14/89 15.7 (9.4-22.1)	22/88 25.0 (17.4-32.6)	0.64 (0.39-1.05)	0.138
MAKE 90 days (20 % eGFR cutoff)	11/89 12.4 (6.6-18.1)	18/88 20.5 (13.4-27.5)	0.61 (0.35-1.08)	0.150
MAKE 90 days (25 % eGFR cutoff)	6/89 6.7 (2.4-11.1)	14/88 15.9 (9.5-22.3)	0.41 (0.19-0.88)	0.047
MAKE 90 days (30 % eGFR cutoff)	4/89 4.5 (0.9-8.1)	14/88 15.9 (9.5-22.3)	0.30 (0.13-0.70)	0.010



MAKE, major adverse kidney events; eGFR, estimated glomerular filtration rate

Source: post-hoc analyses of Study 21-ROS-05

GUARD THERAPEUTICS

Clinical development plan including Phase 2b dose-finding study POINTER

LATE PHASE DEVELOPMENT PLAN VETTED WITH FDA

- FDA (type C) meeting in December 2023 with favorable outcome
- Recognition of current efficacy data
  eGFR (kidney function) & MAKE90
- Confirmation of Fast Track Designation status
  Indication eligible for Breakthrough Therapy Designation
- Agreement on proposed design elements of Phase 2b study (POINTER)
- Fruitful discussion on Phase 3 endpoint – to be continued after Phase 2b
  - Confirmation of a single pivotal Phase 3 study to support NDA
  - Potential for accelerated approval based on interim analysis of eGFR

eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney outcomes; NDA, new drug application

GUARD THERAPEUTICS

PHASE 2B (POINTER) STUDY – OVERVIEW

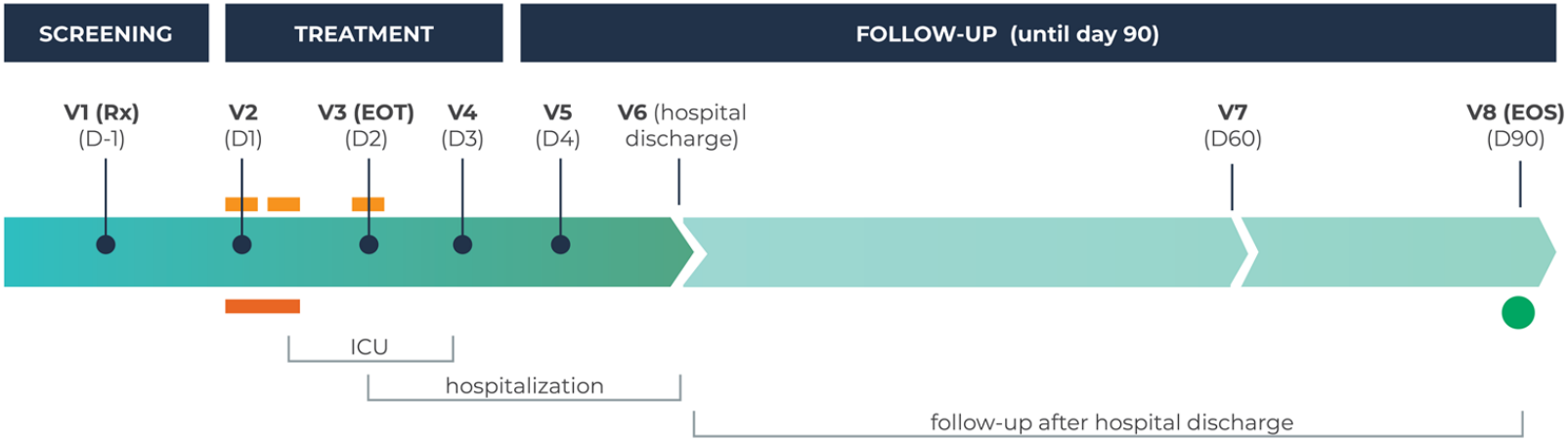
- Global study, run under an US IND
  - Recruitment in Europe & Canada
- Sample size ~ 160 patients
- Two dose arms (60 & 30 mg) & Placebo (2:2:3 randomization)
  - Three drug administrations (surgical dose, 6 & 24 h after first dose)
- Study preparations progress well – first regulatory approval in April 2024 (Health Canada)
- First patient enrollment expected in Q3 2024
- Expected recruitment time ~ 1 year

IND, investigational new drug

GUARD THERAPEUTICS

PHASE 2B (POINTER) – STUDY SCHEME

Principal focus is kidney outcomes on Day 90



Rx = randomization
EOT = end-of-treatment
EOS = end-of-study

- study visit
- administration of study drug
- cardiac surgery
- primary endpoint evaluation

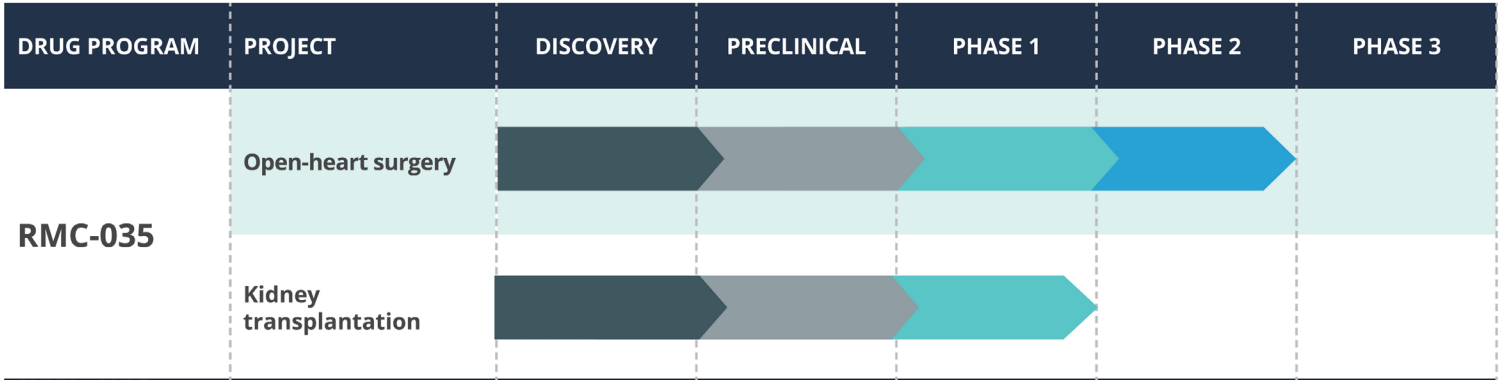
eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney events

Key endpoints:

Primary: change of renal function (eGFR) from baseline to Day 90

Secondary: MAKE90

SECOND CLINICAL PROGRAM – KIDNEY TRANSPLANTATION



- Treatment objective: improve long-term graft function in kidney transplant recipients
- Phase 1b PK/safety study completed
- Further development considered after establishment of optimal dose in heart surgery

Market, competition, IP

GLOBAL MARKET OPPORTUNITY IN HEART SURGERY >1B USD

- Market opportunity in lead indication alone >USD 1bn
  - Target population – open heart surgery (CABG and/or valve) with increased risk for kidney injury
  - Total US population ~250,000 patients
  - Addressable US patient population ~100,000 patients (~30,000 CKD patients)
  - Price potential with current TPP ~USD 5-7.5k per patient (conservative estimate)
  - Total US addressable market opportunity ~USD 500-750m
  - Global addressable market opportunity >USD 1bn
- Additional market opportunities in related acute settings (eg kidney transplantation)
- Preclinical peptide platform suitable for chronic administration, addressing even larger market opportunities in CKD and non-renal indications (multi-billion USD market)
  - Eg diabetic kidney disease, FSGS, IgAN, Alport syndrome

CABG, coronary artery by-pass graft; CKD, chronic kidney disease; TPP, target product profile MoA, mechanism-of-action; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy

Sources: External analysis (draft report, September 2022) & prior work, expert/P&T member interviews; HCUP 2019, J Thorac Dis. 2018 Mar; 10(3): 1960–1967;); 2. Pickering JW et al. Acute kidney injury and prognosis after cardiopulmonary bypass: a meta-analysis of cohort studies, Am J Kidney Dis. 2015 Feb; Epidemiology data on file

COMPETITOR LANDSCAPE – FIRST-TO-MARKET POTENTIAL WITH NO CURRENTLY APPROVED THERAPIES

COMPANY (DRUG)	PHASE	MODE OF ACTION	PROOF-OF-CONCEPT DATA (HEART SURGERY)
Guard Therapeutics (RMC-035)	**2b**	A1M analog	✓
Novartis (TIN816)	**2a**	Human CD39 enzyme	X
AZ/Alexion (Ultomiris)	**3***	C5 inhibitor	X
AM Pharma (Ilofotase alfa)	**2****	Human alkaline phosphatase	X
Renibus Therapeutics (RBT-1)	**2-3*****	Iron sucrose + stannus protoporphyrin	-

*No clinical data in CS-AKI. Drug already approved for PNH and aHUS; Pivotal P3 study in CS-AKI started in Q3 2023.
** Drug failed in sepsis-AKI; announced intent to change indication to CS-AKI
*** Drug targets acute endpoints like dialysis and length of hospital stay. Did not show efficacy on AKI in Phase 2 study

SOLID IP POSITION

- Composition-of-Matter (CoM) patents until 2037, covering RMC-035 & related variants obtained in all major markets (eg, US, EU, Japan, China)
- Possibility for up to 5 years patent extension
- Additional medical use patents with expiry 2029-2037
- Filed patents within GTX platform with expiry 2044
  - CoM & Medical Use

CoM, composition of matter

Preclinical R&D – GTX platform

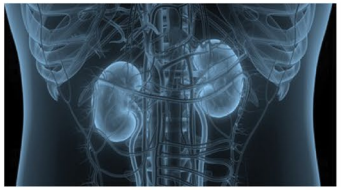
GTX PLATFORM – SUMMARY & OBJECTIVES

- Novel proprietary short peptides with same MoA as RMC-035
- Enables therapeutic potential in chronic setting
  - Kidney (eg DKD, FSGS, IgAN, Alport)
  - Non-kidney (eg hemolytic disorders, vascular diseases)
- Preclinical PoC established in multiple kidney disease models
- Clinically validated MoA for kidney protection in Phase 2 AKITA study – translational confidence with de-risked development in CKD
- Opportunity for MoA-driven patient selection
- Significant commercial opportunity with blockbuster potential
- Candidate drug nomination pending

MoA, mechanism-of-action; DKD, diabetic kidney disease; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; CKD, chronic kidney disease; PoC, proof-of-concept

POSITIONING & OPPORTUNITIES FOR GTX PEPTIDES

RMC-035

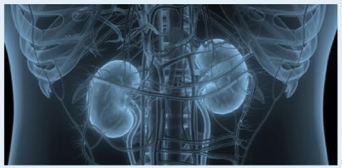


ACUTE KIDNEY INJURY

EXAMPLES OF POTENTIAL USE

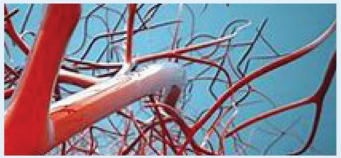
GTX-PEPTIDES

GTX-x



CHRONIC KIDNEY DISEASE

GTX-y



VASCULAR DISORDERS

GTX-z

HEMOLYTICAL DISORDERS

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