Redefining Kidney Disease Treatment with A1M Therapies

Non-confidential summary

September 2025

GUARD THERAPEUTICS

GUARD THERAPEUTICS – EXECUTIVE SUMMARY

RMC-035 for kidney protection in open-heart surgery

- **Phase 2b POINTER study** – **topline results in Q4 2025** (enrollment completed, 170 patients)
- **Clinical proof-of-concept** in Phase 2a AKITA study with 177 patients
  - 59% risk reduction vs placebo (MAKE, regulatory endpoint)
- **FDA Fast Track Designation** (kidney protection in open-heart surgery); eligible for Breakthrough Therapy Designation
- **First-to-market potential** in open-heart surgery; >USD 1 billion market – no approved therapies

Additional opportunities with RMC-035 & GTX peptides

- **Phase 3-ready sepsis program** with additional expansion opportunities (>USD 5 billion market)
- **Preclinical GTX peptides** with broad opportunities in late-stage & orphan chronic kidney diseases (>USD 8 billion market)

Company & Ownership

- Listed on Nasdaq First North Growth Market (Stockholm: GUARD)
- Strong institutional shareholders including Industrifonden & Swedbank Robur

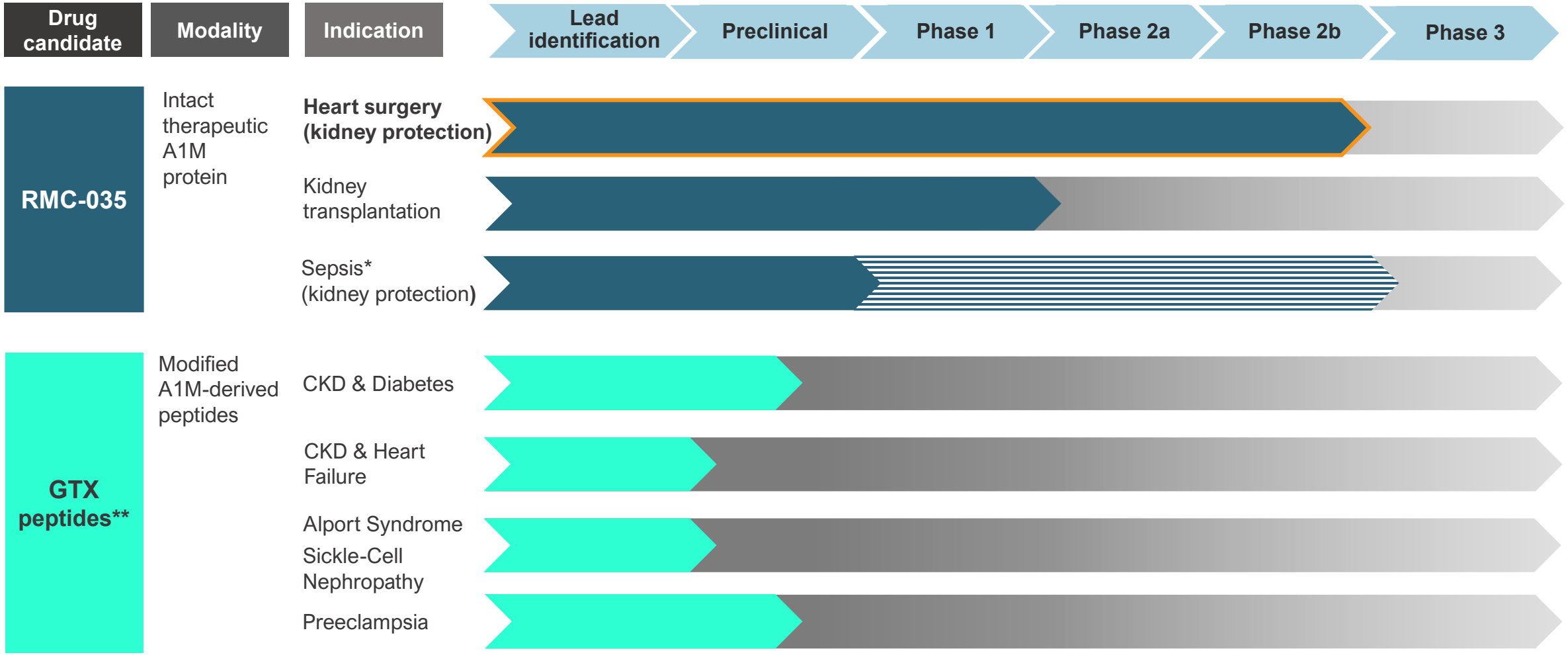
GUARD THERAPEUTICS

EXPERIENCED MANAGEMENT TEAM

– STRONG AND PROVEN TRACK RECORD IN DRUG DEVELOPMENT

NAME / POSITION	EXPERIENCE	NAME / POSITION	EXPERIENCE
 **TOBIAS L. AGERVALD** **CEO** MD, PhD	**+15** years in industry astellas	 **KARIN BOTHA** **CFO** MSc	**+25** years in industry NOVARTIS, SmithKline Beecham, gsk GlaxoSmithKline
 **MICHAEL REUSCH** **CMO** MD	**+30** years in industry Fujisawa, astellas	 **PETER GILMOUR** **CSO/Head of Preclinical** MSc, PhD	**+20** years in industry AstraZeneca, astellas
 **TORBJÖRN LARSSON** **Head of CMC** BSc	**+30** years in industry Medivir, aprea therapeutics, Pharmacia & Upjohn	 **SARA THURESSON** **Head of Clinical Operations** MSc	**+20** years in industry oncopeptides, WILSON THERAPEUTICS, IQVIA, Medivir

BUILDING A DIFFERENTIATED PIPELINE ON A1M'S UNIQUE BIOLOGY



* Opportunity to initiate pivotal Phase 3 study in sepsis following results in ongoing Phase 2b study (POINTER) in open-heart surgery.

** Multiple GTX peptides fulfill criteria for candidate drug nomination. GTX-86 at nomination stage.

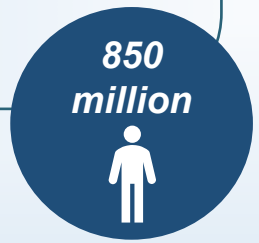
A1M, alpha-1-microglobulin

CHRONIC KIDNEY DISEASE & KIDNEY FAILURE

– A GLOBAL HEALTH CONCERN

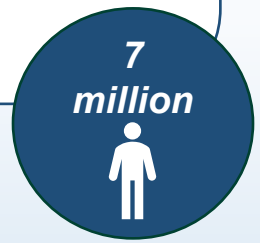
Chronic Kidney Disease

- Severe complications, including cardiovascular disease and kidney failure
- Years of life lost from CKD expected to soon surpass diabetes



Kidney failure

- Requires dialysis or kidney transplantation – poor outcomes and high cost
- High annual mortality rate (15-20%), worse than many cancers



Significant healthcare costs for kidney failure

~7% of Medicare budget, ~1% of Medicare population

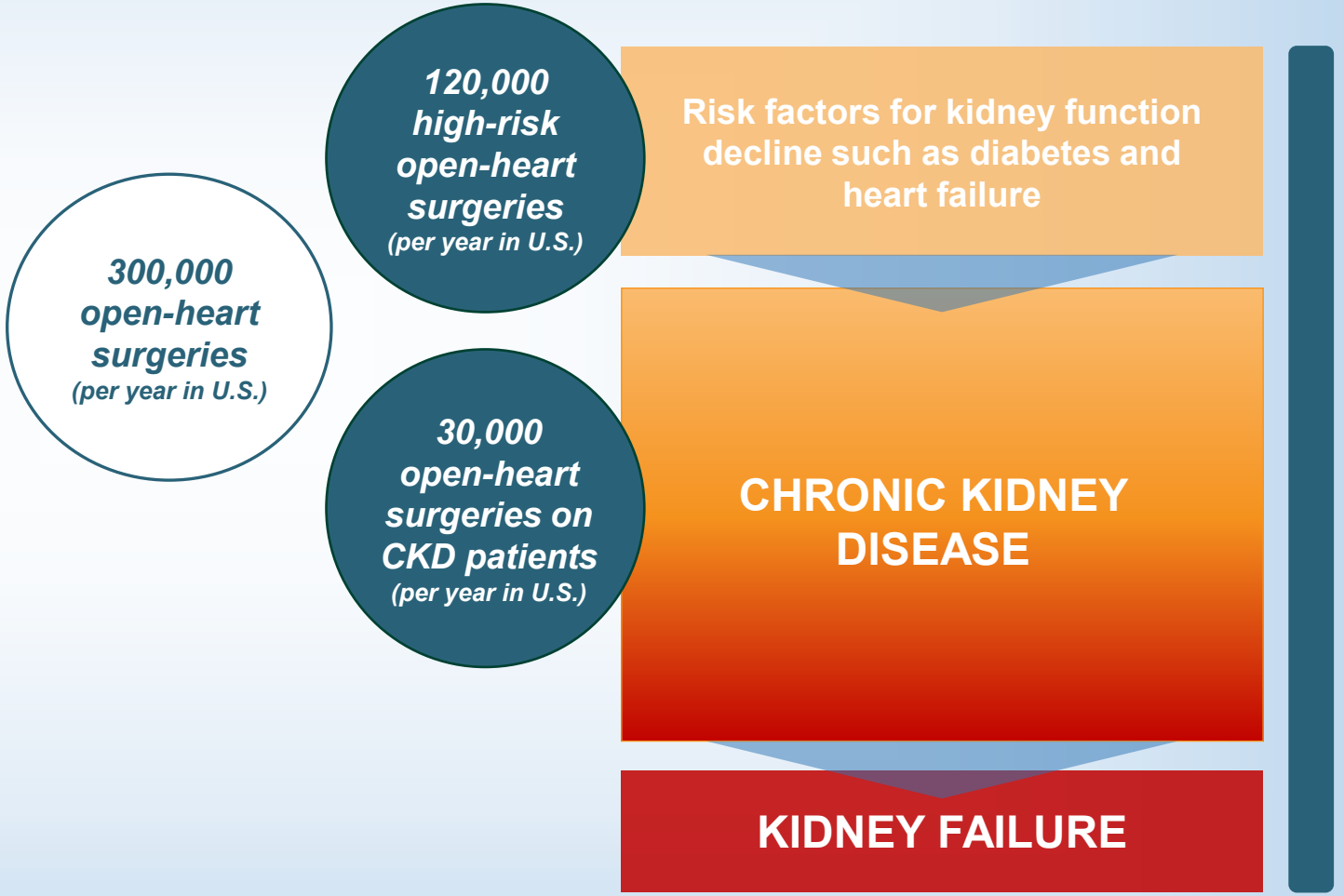
>USD 50 billion in Medicare annual spend

Francis et al, Nature Reviews Nephrology 2024, P Stenvinkel and TE Larsson, Am J Kidney Dis, 2013 Aug;62(2):339-51
2021 USRDS Annual Data Report July 2024 Data Book: Health Care Spending and the Medicare Program – MedPAC
GBD Chronic Kidney Disease Collaboration; Volume 395, Issue 10225 p709-733 February 29, 2020

HEART SURGERY AND THE LASTING BURDEN OF KIDNEY DISEASE

Open-heart surgery poses a high risk for irreversible loss of kidney function –

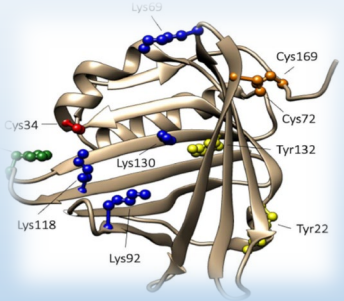
Protecting the kidneys during open-heart surgery will reduce the burden of Chronic Kidney Disease



Chawla, L. S., & Kimmel, P. L. (2012). Acute kidney injury and chronic kidney disease: an integrated clinical syndrome. Kidney International, 82(5), 516-524
Global Data (2025)
Real-world data (Cerner database, internal data on file)

A1M TARGETS CORE MECHANISMS OF KIDNEY INJURY IN OPEN-HEART SURGERY

Injury type	*Molecular action*	*Protective effect*
Ischemia – reperfusion	Reductase activity* Radical scavenging**	Reduces oxidative injury Preserves tissue integrity
Hemolysis	Heme-binding & neutralization***	Reduces heme-driven cell injury
Mitochondrial dysfunction	Cytochrome C binding & stabilization	Improves mitochondrial function & respiration



Each A1M molecule:

* Reduces 5-6 free radicals
** Traps 3-4 radicals
*** 2 heme-binding sites

A1M, alpha-1-microglobulin

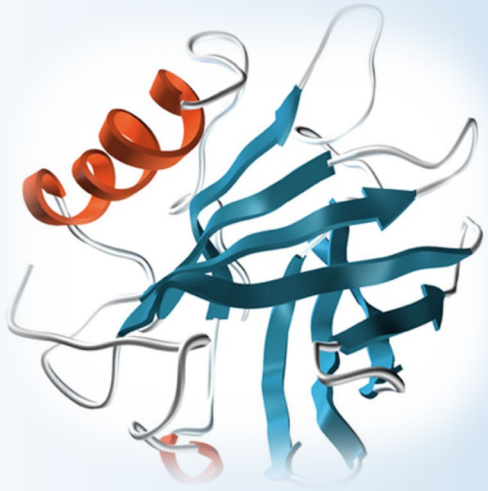
Bergwik et al., Front Physiol 2021

RMC-035 – FIRST-IN-CLASS THERAPY FOR ACUTE KIDNEY INJURY

Harnessing endogenous A1M defense
Protects kidney function at the core mechanism of injury

Protein replacement therapy
Clinically validated concept with first-in-class potential

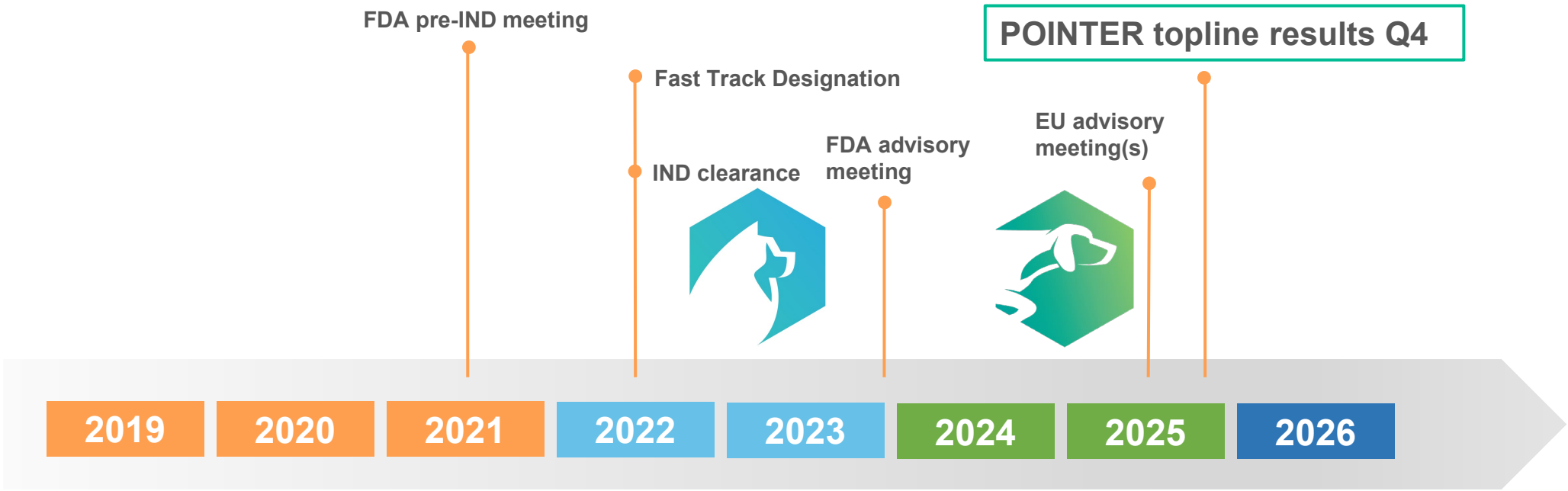
Simple hospital delivery
Short-term IV infusion, seamlessly integrated into standard care



A1M, alpha-1-microglobulin

Bergwik et al., Front Physiol 2021

SUCCESFULLY DELIVERING ON CLINICAL & STRATEGIC PLAN



Clinical Phase 1 program

- ✓ ROS-01 (single dose, healthy subjects)
- ✓ ROS-02 (multiple doses, healthy subjects)
- ✓ ROS-03 (renal impairment study)
- ✓ ROS-04 (safety/PK study in heart surgery)

Phase 2a *AKITA* study

- ✓ ROS-05 (proof-of-concept, heart surgery)

Phase 1b study

- ✓ ROS-06, kidney transplant

Phase 2b *POINTER* study

ROS-07 (dose-finding)

Phase 3 study heart surgery

Optional Phase 3 study in sepsis

PROMISING EFFICACY DATA IN PHASE 2a *AKITA* STUDY

Placebo-controlled, 177 patients undergoing open-heart surgery

Statistically significant & clinically meaningful improvement of kidney function (90 days after surgery)

eGFR benefit vs placebo

4.3 mL/min (total population)

7.9 mL/min (CKD subgroup)

MAKE* Relative Risk Reduction

59%

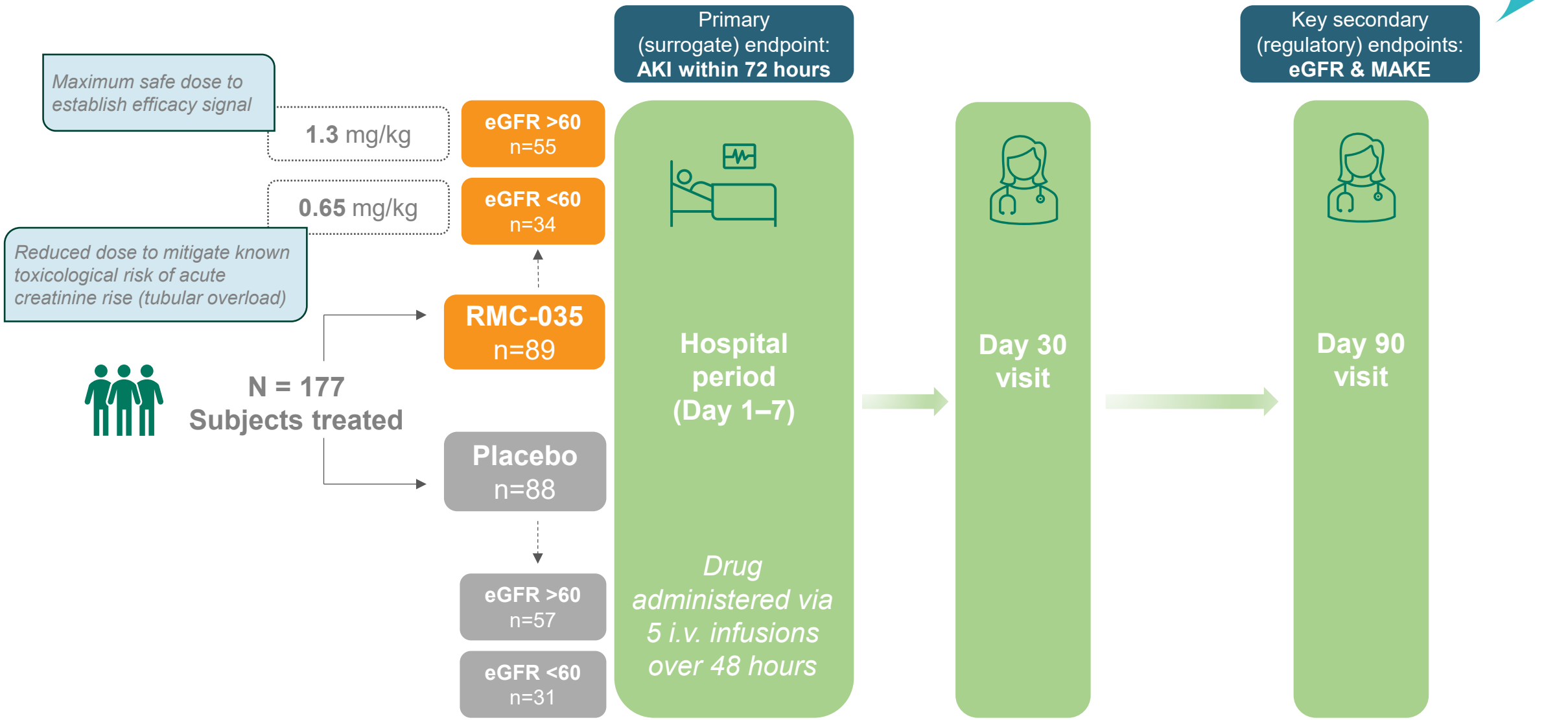
→ Phase 3 endpoint for market approval

Robust kidney protection profile – positions RMC-035 for late-stage clinical development

**MAKE = major adverse kidney event*
*Composite of **death, dialysis, or ≥ 25% eGFR decline***

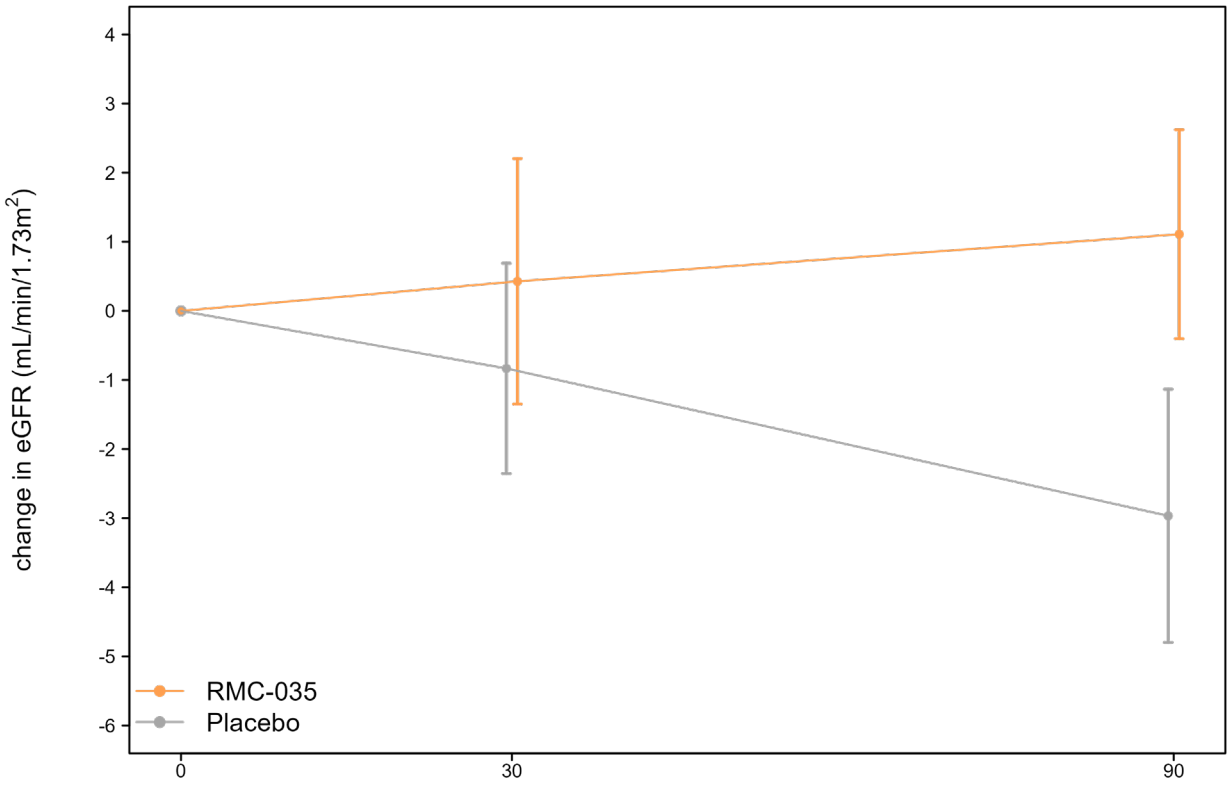
Zarbock et al. eClinicalMedicine, 2024 Sep 16:76:102830

PHASE 2a *AKITA* STUDY – OVERVIEW



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

RMC-035 PREVENTS LOSS OF RENAL FUNCTION AFTER OPEN-HEART SURGERY – eGFR ENDPOINT



eGFR endpoint at Day 90 met

4.3 mL/min
P=0.06

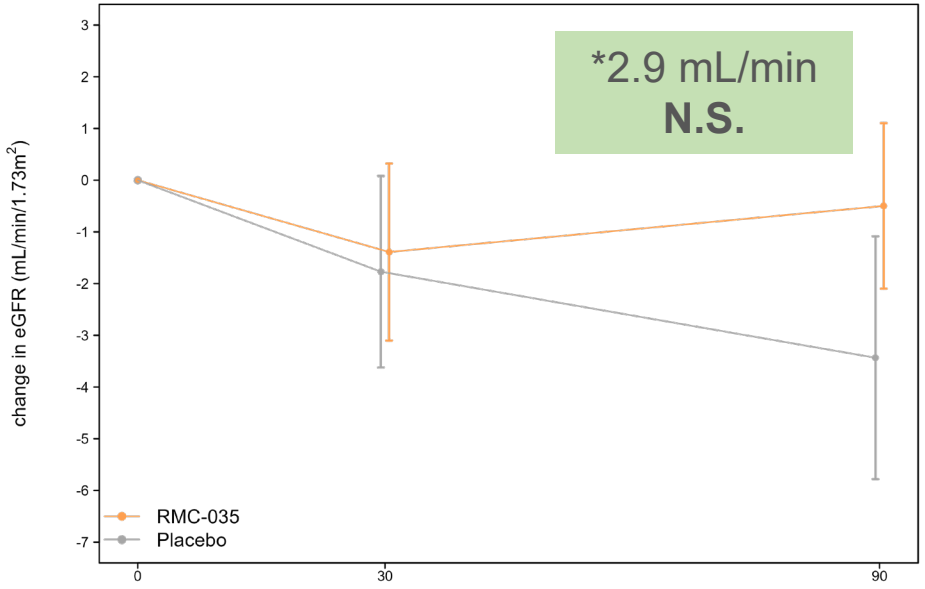
Pre-defined two-sided alpha is 0.1
P-values < 0.1 are statistically significant

Source: Study 21-ROS-05 CSR; Error bars indicate mean +/- Standard Error; eGFR change assessed by a Mixed Model of Repeated Measures

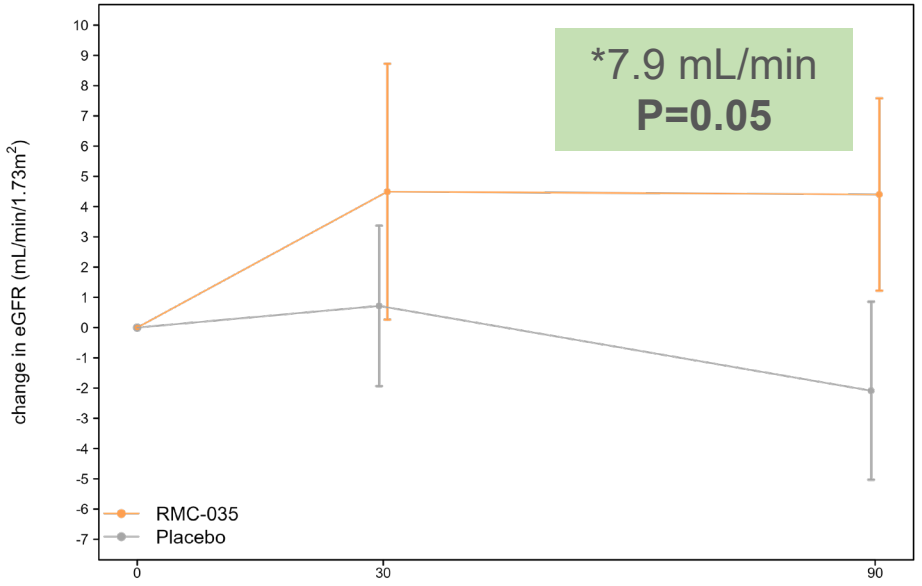
RMC-035 PREVENTS LOSS OF RENAL FUNCTION AFTER OPEN-HEART SURGERY – eGFR SUBGROUP ANALYSIS

Pre-specified eGFR subgroups based on dose and kidney injury risk

eGFR ≥ 60 (dose 1.3 mg/kg)



eGFR < 60 (0.65 mg/kg)

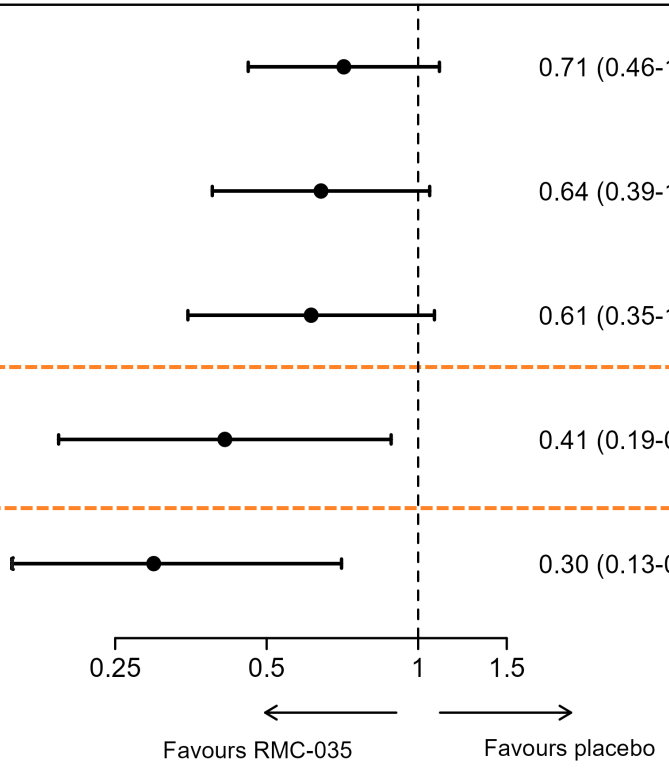


eGFR endpoint met in subgroup eGFR < 60

Source: Study 21-ROS-05 CSR; Error bars indicate mean +/- Standard Error; eGFR change assessed by a Mixed Model of Repeated Measures*

RMC-035 CONSISTENTLY REDUCES REGULATORY ENDPOINT MAKE90 ACROSS THRESHOLDS OF eGFR LOSS

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



MAKE90 endpoint met

Source: Study 12-ROS-05 CSR & post-hoc analyses of Study 21-ROS-05. MAKE, major adverse kidney events; eGFR, estimated glomerular filtration rate

PHASE 2b *POINTER* STUDY – RESULTS IN Q4 2025

Key Design Elements

- 170 patients enrolled (EU & Canada)
- Two RMC-035 dose groups (30 & 60 mg) and placebo (2:2:3 randomization)
- Three doses administered over 24 hours
- Primary endpoint: change in renal function (eGFR) from pre-surgery to Day 90
- Powered to detect eGFR difference of 5 mL/min with two-sided alpha of 0.1

Key milestones achieved

- ✓ Patient enrollment completed in 9 months – ahead of plan
- ✓ Independent interim safety reviews with positive outcome
- ✓ Data collection near completion

Topline results expected in Q4

PIVOTAL PHASE AHEAD – KEY VALUE DRIVERS

Q4 2025 → H1 2026

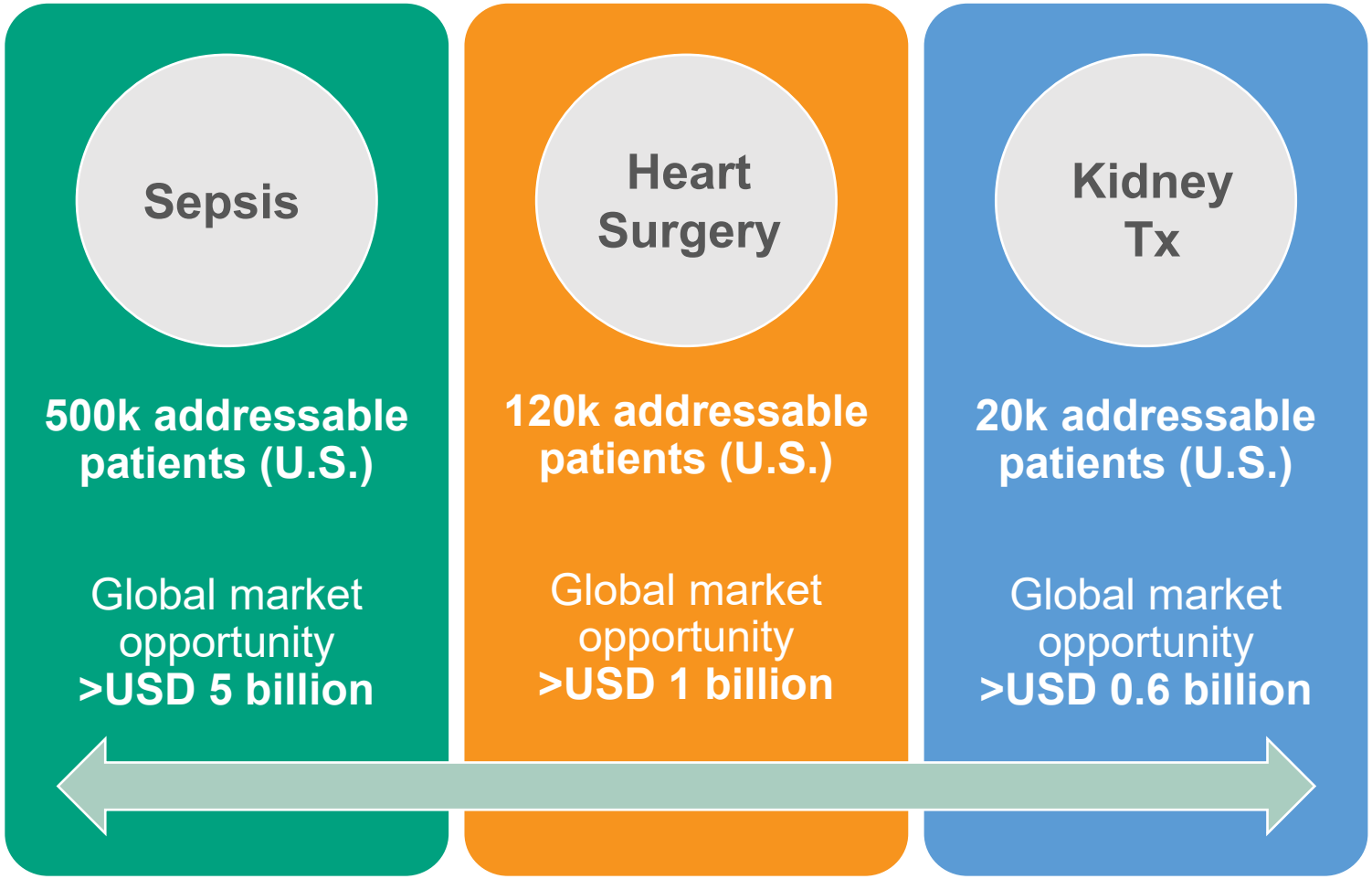
POINTER results

- Breakthrough Therapy Application
- Clinical End-of-Phase 2 FDA meeting
- Phase 3 preparations & BD opportunities

FIRST-TO-MARKET POTENTIAL – NO APPROVED THERAPIES

COMPANY (DRUG)	PHASE	MECHANISM	EFFICACY DATA IN HEART SURGERY	COMMENT
Guard Therapeutics (RMC-035)	**2b**	**A1M analogue**	**Yes**	eGFR & MAKE benefit in Phase 2 AKITA study Phase 2b POINTER results expected Q4 2025
AM Pharma (Ilofotase alpha)	2	ALP analogue	-	Study start Q4 2023, expected completion Q3 2025
AstraZeneca / Alexion (Ultomiris)	3	Complement 5 inhibitor	-	Study start Q2 2023, expected completion Q1 2027
Genentech (GDC-8264)	2a/b	RIP-1 inhibitor	-	Study start Q1 2025, expected completion Q4 2027
Novartis (TIN-816)	2a	Human CD39 enzyme	-	Study recently stopped due to lack of efficacy
Renibus Therapeutics (RBT-1)	*3*	*Iron sucrose + stannus protoporphyrin*	-	*Focus on acute outcomes. No efficacy on kidney endpoints in Phase 2*

GLOBAL MARKET OPPORTUNITY POSITIONS RMC-035 FOR BLOCKBUSTER POTENTIAL



External analysis (September 2022) & interviews with Health Care Professionals & Hospital & Therapeutics Committee members.
Data from US Renal Data System (USRDS) & Organ Procurement and Transplantation Network (OPTN)
US CDC website
Rhee at al. Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014

RECENT PHARMA DEALS IN NEPHROLOGY
– TOTAL DEAL VALUE OVER $12BN 2023-25 YTD

TARGET	ACQUIRER	YEAR	DEAL VALUE	STAGE	LEAD ASSET	INDICATION
Regulus Tx	Novartis	2025	**$800m + $900m milestones**	Phase 1b	Farabursen	Autosomal Dominant Polycystic Kidney Disease
Alpine Immune Sciences	Vertex Pharma	2024	**$4.9bn**	Phase 2	Povetacicept	IgAN
Human Immunology Biosciences	Biogen	2024	**$1.15bn + milestones**	Phase 2	Feltzartamab	IgAN, Primary membranous nephropathy & antibody-mediated rejection
Jnana Tx	Otsuka	2024	**$800m**	Preclinical	Panel of solute carrier inhibitors	Ion transporter kidney disease
Calliditas	Asahi Kasei	2024	**$1.1bn**	Marketed	Tarpeyo (Budesonide)	IgAN
Chinook Tx	Novartis	2023	**$3.5bn**	Phase 3	Atrasentan & Zigakibart	IgAN
CinCor Pharma	AstraZeneca	2022	$1.8bn	Phase 2	Baxdrostat	Treatment-resistant hypertension, primary aldosteronism and CKD
Vifor Pharma	CSL	2021	$12.3bn	-	Product portfolio in nephrology	-
Sanifit Tx	Vifor Pharma	2021	$205m + milestones	Phase 3	SNF472	Treatment for calciphylaxis ESRD patients
Corvidia Tx	Novo Nordisk	2020	$2.1bn	Phase 2	Zilitivekimab	Therapies within CKD segments

GTX peptides –

Broadening the A1M Platform Beyond Acute Indications

GUARD THERAPEUTICS

GTX PEPTIDES – NEXT GENERATION A1M PLATFORM

Expanding A1M Biology Into New Frontiers

Scientific foundation

- Novel A1M-derived peptides with preserved functionality, potency comparable to native A1M
- ~15–35 aa, synthetically manufactured
- Robust preclinical efficacy across diverse acute and chronic models

Strategic positioning

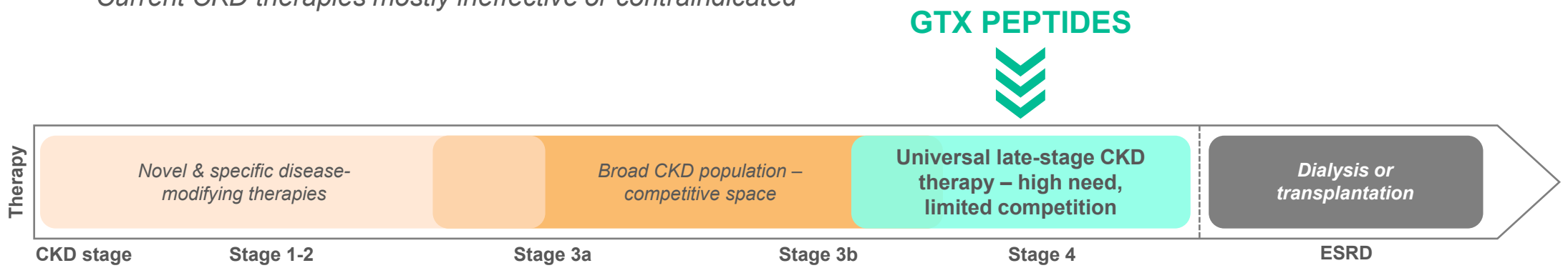
- Strong IP (composition of matter until 2044)
- Broad clinical development opportunity with unique positioning in CKD
- High optionality – strategy under refinement

Path to clinic

- Lead candidates identified
- ~2 years to IND filing

GTX PEPTIDES – MASSIVE OPPORTUNITY IN LATE-STAGE CKD

- **A1M mechanism validated** in numerous disease models, e.g., kidney disease and preeclampsia
- **Broad impact across CKD,** including orphan diseases
  - *Robust efficacy in a wide range of preclinical kidney disease models*
- **Specific opportunity in late-stage CKD**
  - *Highest risk for progression to kidney failure (end-stage renal disease, ESRD)*
  - *Often excluded from clinical trials*
  - *Current CKD therapies mostly ineffective or contraindicated*



CKD classification based on Kidney Disease Improving Global Outcomes (KDIGO); CKD, chronic kidney disease

GUARD THERAPEUTICS – EXECUTIVE SUMMARY

RMC-035 for kidney protection in open-heart surgery

- **Phase 2b POINTER study** – **topline results in Q4 2025** (enrollment completed, 170 patients)
- **Clinical proof-of-concept** in Phase 2a AKITA study with 177 patients
  - 59% risk reduction vs placebo (MAKE, regulatory endpoint)
- **FDA Fast Track Designation** (kidney protection in open-heart surgery); eligible for Breakthrough Therapy Designation
- **First-to-market potential** in open-heart surgery; >USD 1 billion market – no approved therapies

Additional opportunities with RMC-035 & GTX peptides

- **Phase 3-ready sepsis program** with additional expansion opportunities (>USD 5 billion market)
- **Preclinical GTX peptides** with broad opportunities in late-stage & orphan chronic kidney diseases (>USD 8 billion market)

Company & Ownership

- Listed on Nasdaq First North Growth Market (Stockholm: GUARD)
- Strong institutional shareholders including Industrifonden & Swedbank Robur

GUARD THERAPEUTICS

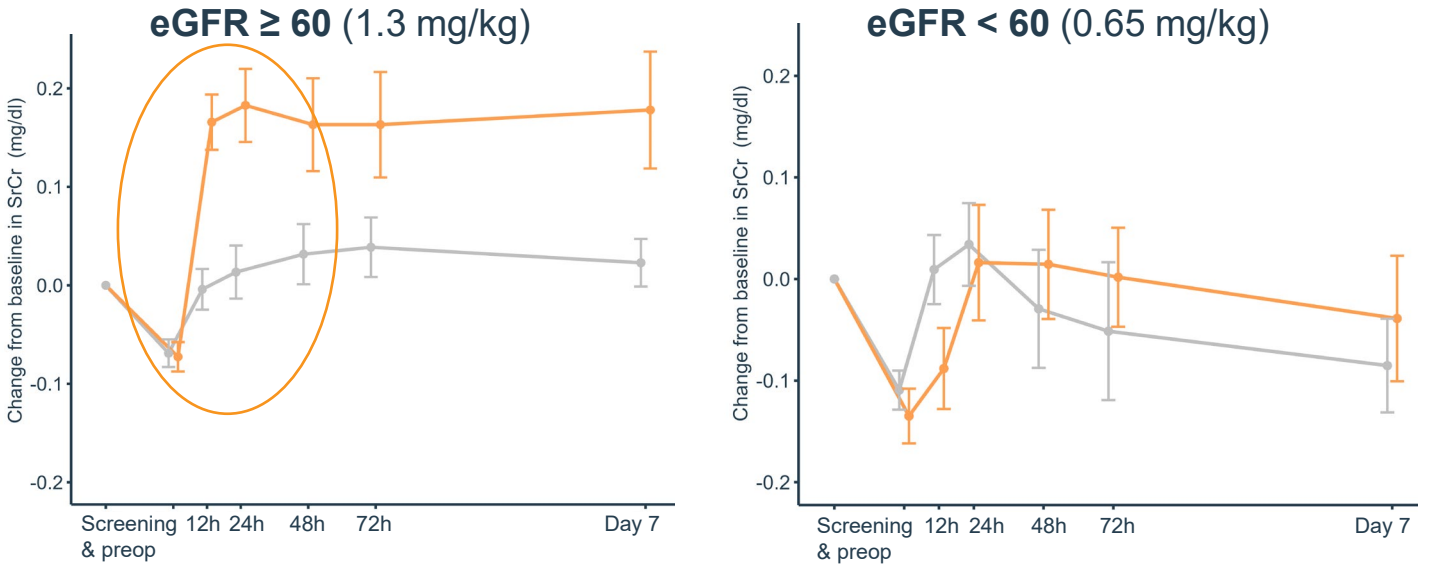
Appendix

GUARD THERAPEUTICS

AKI ENDPOINT – ASSESSMENT CONFOUNDED BY ACUTE CREATININE RISE IN HIGH DOSE GROUP

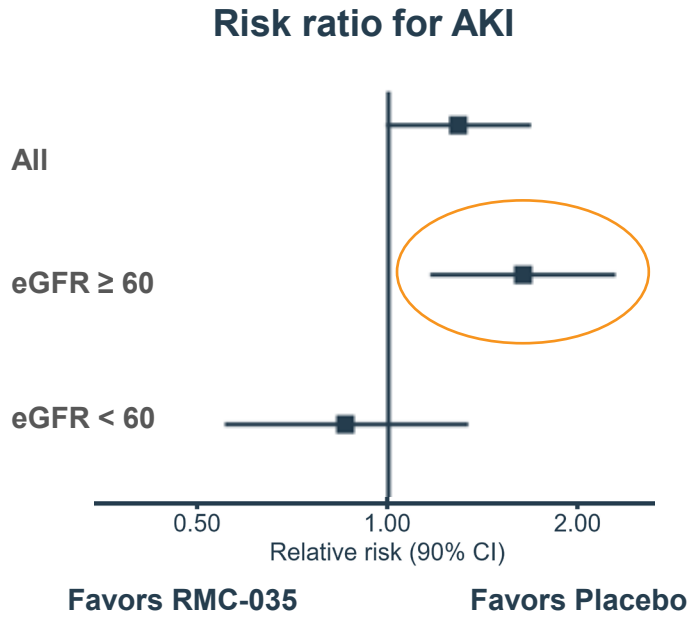
- No significant difference in AKI rate (*RR 1.30, p=0.12*)
- Higher AKI rate with RMC-035 in subgroup eGFR ≥60 (*RR 1.66, p=0.015*) **consistent with exposure-driven acute creatinine rise**

Post-operative change in creatinine to Day 7 by eGFR subgroup



Acute, reversible creatinine increase with high dose – above exposure threshold for tubular overload

No acute creatinine increase with low dose – below exposure threshold for tubular overload

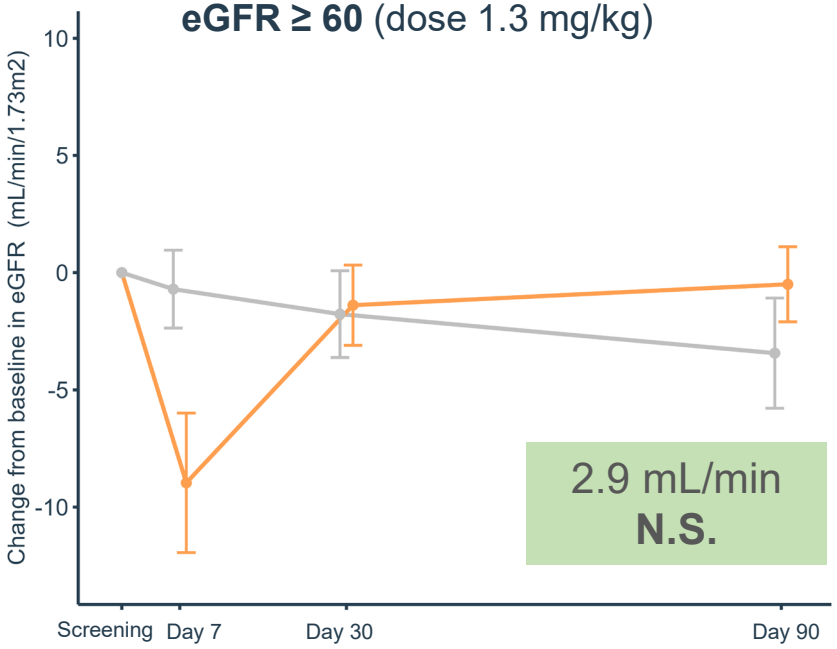


Source: Study 21-ROS-05 CSR; error bars indicate mean +/- Standard Error (SE); AKI assessed according to KDIGO criteria based on serum creatinine (SCr)

RMC-035 PREVENTS LOSS OF RENAL FUNCTION AFTER OPEN-HEART SURGERY: eGFR SUBGROUP ANALYSIS

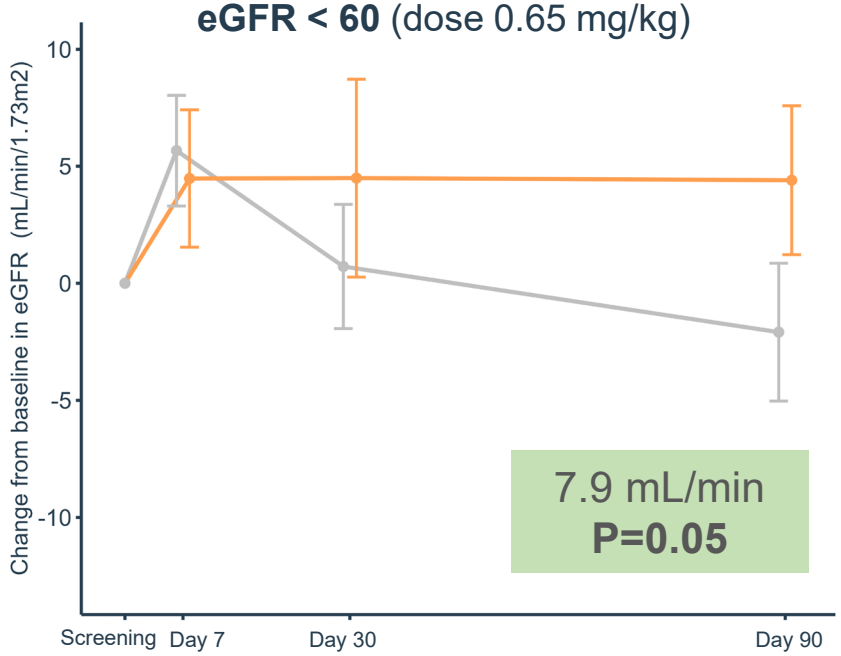
Pre-specified eGFR subgroups based on dose and kidney injury risk

eGFR ≥ 60 (dose 1.3 mg/kg)



Efficacy reduced with high dose exceeding exposure threshold for acute creatinine increase (eGFR decline)

eGFR < 60 (dose 0.65 mg/kg)



Robust efficacy observed with lower dose not exceeding exposure threshold for acute creatinine increase

eGFR endpoint met in subgroup eGFR < 60

Source: Study 21-ROS-05 CSR; Error bars indicate mean +/- Standard Error; eGFR change assessed by a Mixed Model of Repeated Measures; N.S., not significant

RMC-035 IN SEPSIS – CLEAR PATH FROM UNMET NEED TO PHASE 3

Unmet need

- Sepsis is leading cause of acute kidney injury
- ~1.7M cases/year (U.S.)
- ~800k develop overt kidney injury
- ~250k progress to CKD

Rationale

- Broad endogenous mechanism targeting sepsis-related kidney injury
- Clinical efficacy demonstrated in open-heart surgery
- Preclinical proof-of-concept established

Regulatory Path

- MAKE90 as Phase 3 primary endpoint – aligned with open-heart surgery program
- Single confirmatory Phase 3 trial sufficient for approval
- Bridging Phase 1b PK study to extend systemic exposure

Phase 3 Design

- ~ 400–600 patients
- Recruitment ~2 years

US CDC website
Rhee at al. Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014
Tekeuchi et al. Epidemiology of sepsis-associated acute kidney injury in the ICU with contemporary consensus definitions
Esposito et al, Acute kidney injury in hospitalized patients with real-life analysis of incidence and clinical impact in Italian hospitals (the SIN-AKI study)