Novel therapies targeting kidney disease

Company Presentation

October 2024

GUARD THERAPEUTICS

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PIONEERING TRANSFORMATIVE MEDICINES FOR KIDNEY DISEASE

RMC-035 for **kidney protection** in open heart surgery

- **Phase 2b *POINTER*** study with RMC-035 initiated – **results expected year-end 2025**
- **Granted FDA Fast Track Designation** (kidney protection in open heart surgery); eligible for Breakthrough Therapy Designation
- **Clinical proof-of-concept established in Phase 2a AKITA study with 177 patients**
  - **59% reduction vs placebo (MAKE, regulatory endpoint)**
- **First-to-market potential** in open-heart surgery; >USD 1 billion market – no approved therapies

Additional **opportunities** with RMC-035 & GTX peptides

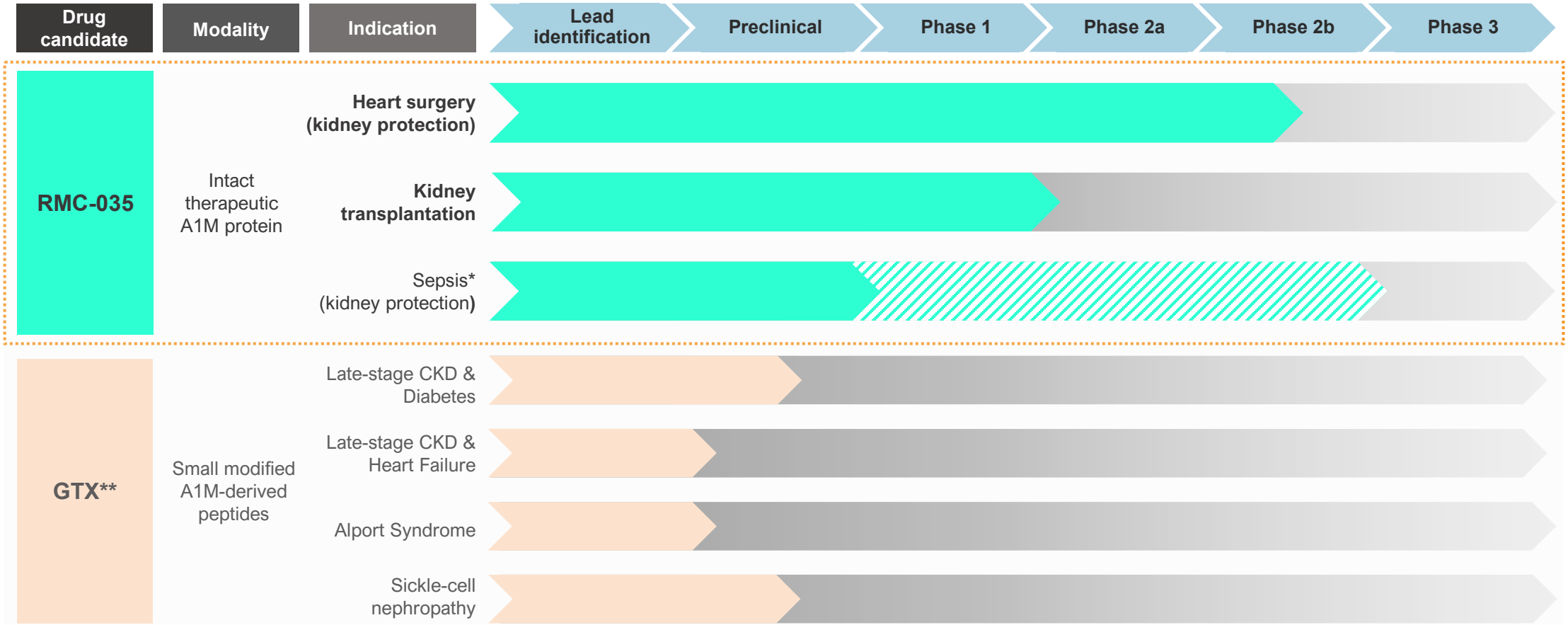
- **Phase 3 ready sepsis programme** and **Phase 2a/b ready kidney transplantation programme** for >USD 5.6 billion market
- **Unique positioning of preclinical GTX peptides** in late stage and orphan chronic kidney diseases for >USD 8 billion market
- Listed in Stockholm with top shareholders including Industrifonden and Swedbank Robur [Nasdaq FN Growth Market: GUARD]

GUARD THERAPEUTICS

EXPERIENCED MANAGEMENT TEAM WITH STRONG & PROVEN TRACK RECORD IN 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, 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, IQVIA, WILSON THERAPEUTICS, Medivir

LATE-STAGE RMC-035 DEVELOPMENT WITH MULTIPLE PIPELINE OPPORTUNITIES



* 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 & END-STAGE RENAL DISEASE – A GLOBAL HEALTH CONCERN

Acute Kidney Injury (AKI):

- Multiple causes, often resulting from in-hospital complications like severe infections & sepsis and major surgeries (e.g., open-heart surgery, kidney transplantation)
- 50% or more of high-risk open-heart surgery patients develop AKI; addressable patient population ~100,000-120,000 cases per year in the US alone (~30,000 patients with pre-operative CKD)

Progression to Chronic Kidney Disease (CKD)

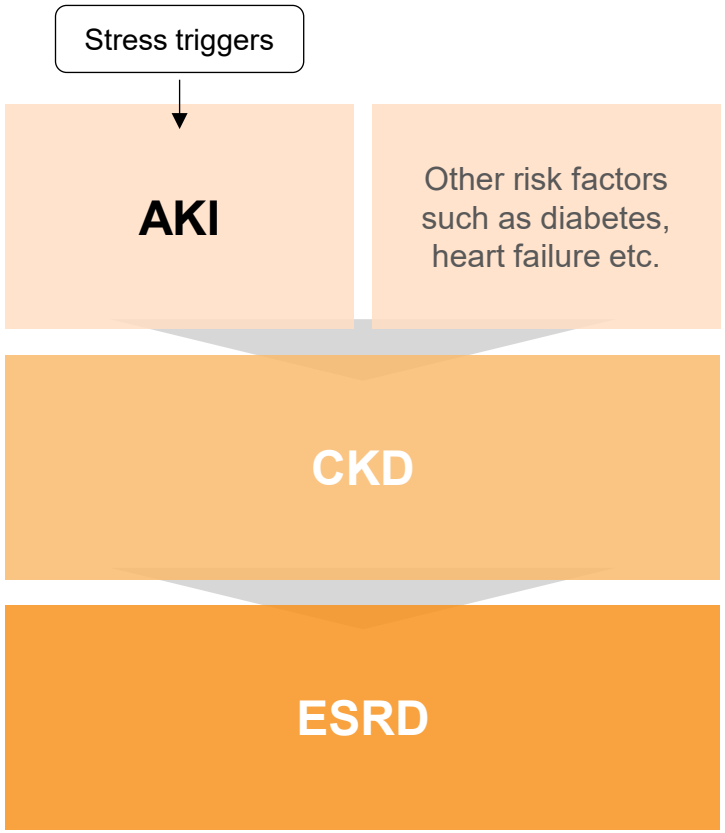
- AKI raises the risk of CKD; 15-20% progress to advanced CKD within 24 months
- CKD leads to severe complications, e.g., cardiovascular disease and kidney failure
- Years of life lost (YLL) from CKD are expected to surpass diabetes by 2040

AKI in patients with pre-existing CKD:

- CKD is a strong risk factor for AKI
- AKI in CKD accelerates progression to ESRD – high unmet need

CKD to End-Stage Renal Disease (ESRD):

- 10-15% of CKD patients advance to ESRD; requires dialysis or kidney transplant
- High mortality rate (15-20%), worse than many cancers
- Represents 7% of Medicare costs but affects 1% of the population

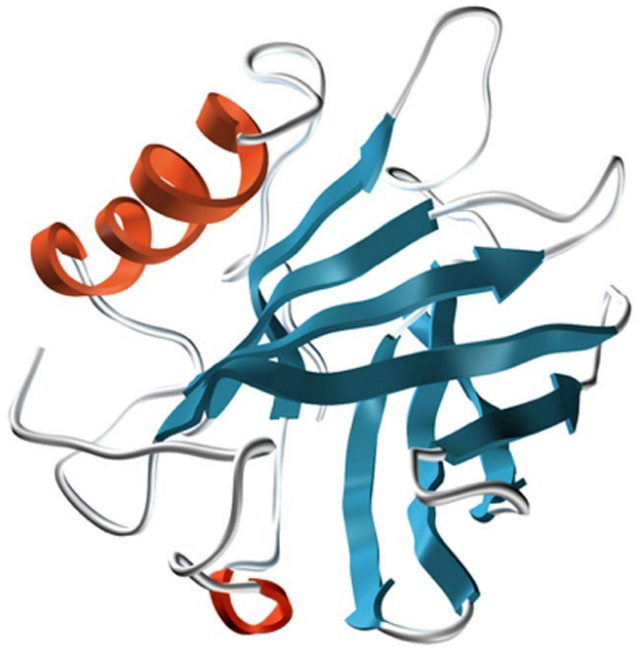


Francis et al, Nature Reviews Nephrology 2024, P Stenvinkel and TE Larsson, Am J Kidney Dis, 2013 Aug;62(2):339-51, 2021 USRDS Annual Data Report
July 2024 Data Book: Health Care Spending and the Medicare Program – MedPAC , Chawla, L. S., & Kimmel, P. L. (2012). Acute kidney injury and chronic kidney disease: an integrated clinical syndrome. Kidney International, 82(5), 516-524

NOVEL THERAPEUTIC APPROACH

Harnessing natural properties of alpha-1-microglobulin (A1M) to protect the kidneys

- **Preferentially distributed to kidney** including proximal tubules
- **Reduces oxidative stress** and **heme toxicity**, two primary triggers in the onset of Acute Kidney Injury (AKI)
- **Eases stress on kidneys** during high-risk situations, such as open-heart surgery, potentially lowering the incidence of AKI in vulnerable patients
- **Supports kidney recovery**, offering a new avenue to prevent the progression of AKI to more severe stages like CKD and ESRD
- Potentially **saving lives** while also **reducing the substantial financial burden** on the healthcare system



3-D structure of A1M protein

A1M PROTECTS KIDNEY FUNCTION BY TARGETING CRITICAL DISEASE PATHWAYS

Challenges	A1M's Key Actions	Protective Effects
Oxidative stress damages kidney cells	**Neutralizes Oxidative Stress**	**Reduces cell injury from ROS and hemolysis**
Hemolysis-induced kidney injury	**Binds & Degrades Free Heme**	**Prevents cell toxicity from free heme / hemoglobin**
Mitochondrial damage and cell death	**Stabilizes Mitochondria**	**Protects mitochondrial integrity**
Inflammatory response after ischemia-reperfusion	**Prevents Secondary Inflammation**	**Reduces inflammatory injury and tissue scarring**

Bergwik et al., Front Physiol 2021

RMC-035 (recombinant alpha-1-microglobulin)

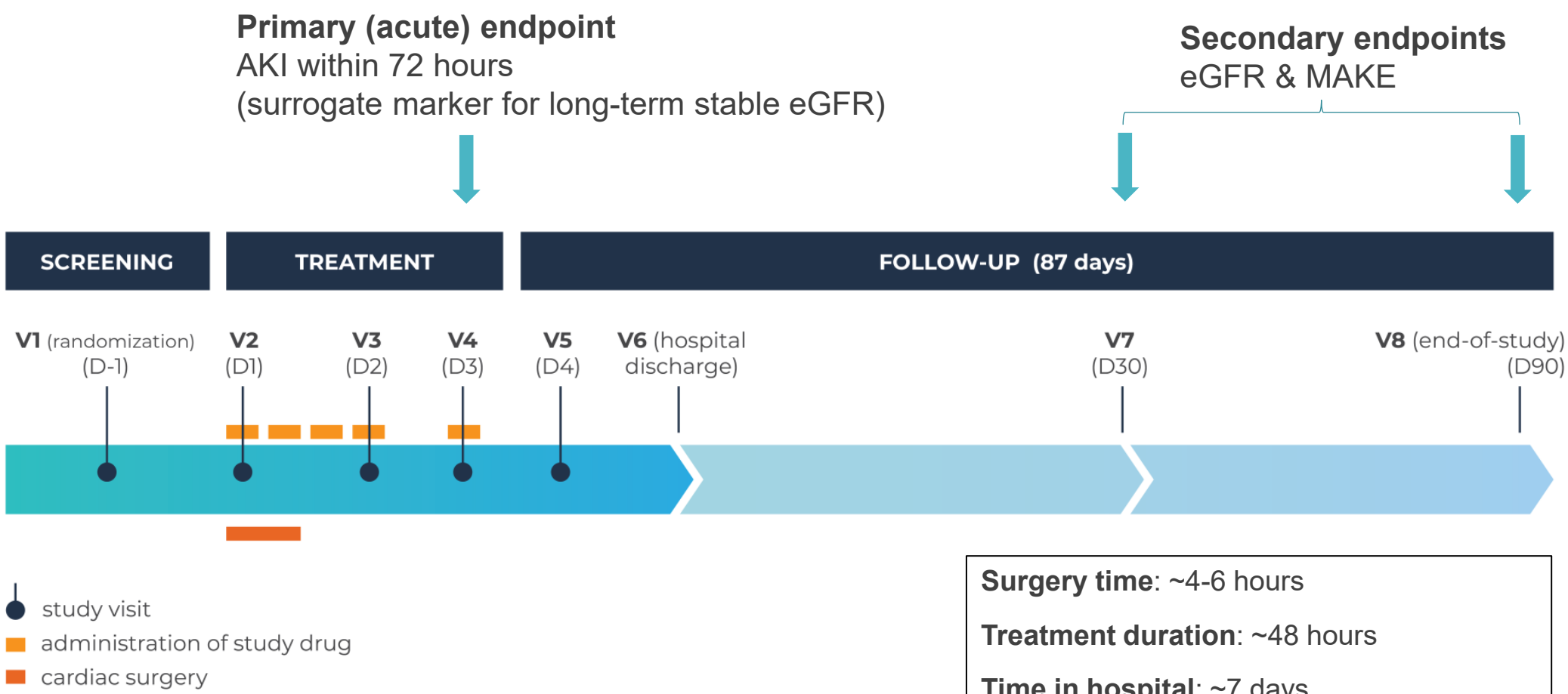
Kidney protection in heart surgery

COMPLETED PHASE 2a *AKITA* STUDY – OUTLINE & OBJECTIVES

- Recruitment in the **US, Canada & Europe**
- Double-blind, placebo-controlled (1:1 RMC-035:placebo) in patients undergoing **open-heart surgery at increased risk for kidney injury**
- Sample size ~170 to maximum 348 subjects
- Main objective: **Proving efficacy** & safety with **the maximum possible dose**
  - *Primary endpoint: Acute eGFR, not accepted for regulatory approval*
  - *Secondary endpoints: Long-term eGFR, accepted for regulatory approval*
- Start dose 1.3 mg/kg; reduced to 0.65 mg/kg for patients with low pre-operative renal function
  - *Overexposure risks linked to short-term eGFR dip*

eGFR, estimated glomerular filtration rate

COMPLETED PHASE 2a *AKITA* STUDY – FLOWCHART



Surgery time: ~4-6 hours

Treatment duration: ~48 hours

Time in hospital: ~7 days

Follow-up time: up to 90 days after surgery

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

PHASE 2a RESULTS SUPPORT ROBUST EFFICACY ON HARD KIDNEY ENDPOINTS

Efficacy stronger than required for regulatory approval based on renal function (eGFR) & Major Adverse Kidney Events (MAKE) on Day 90

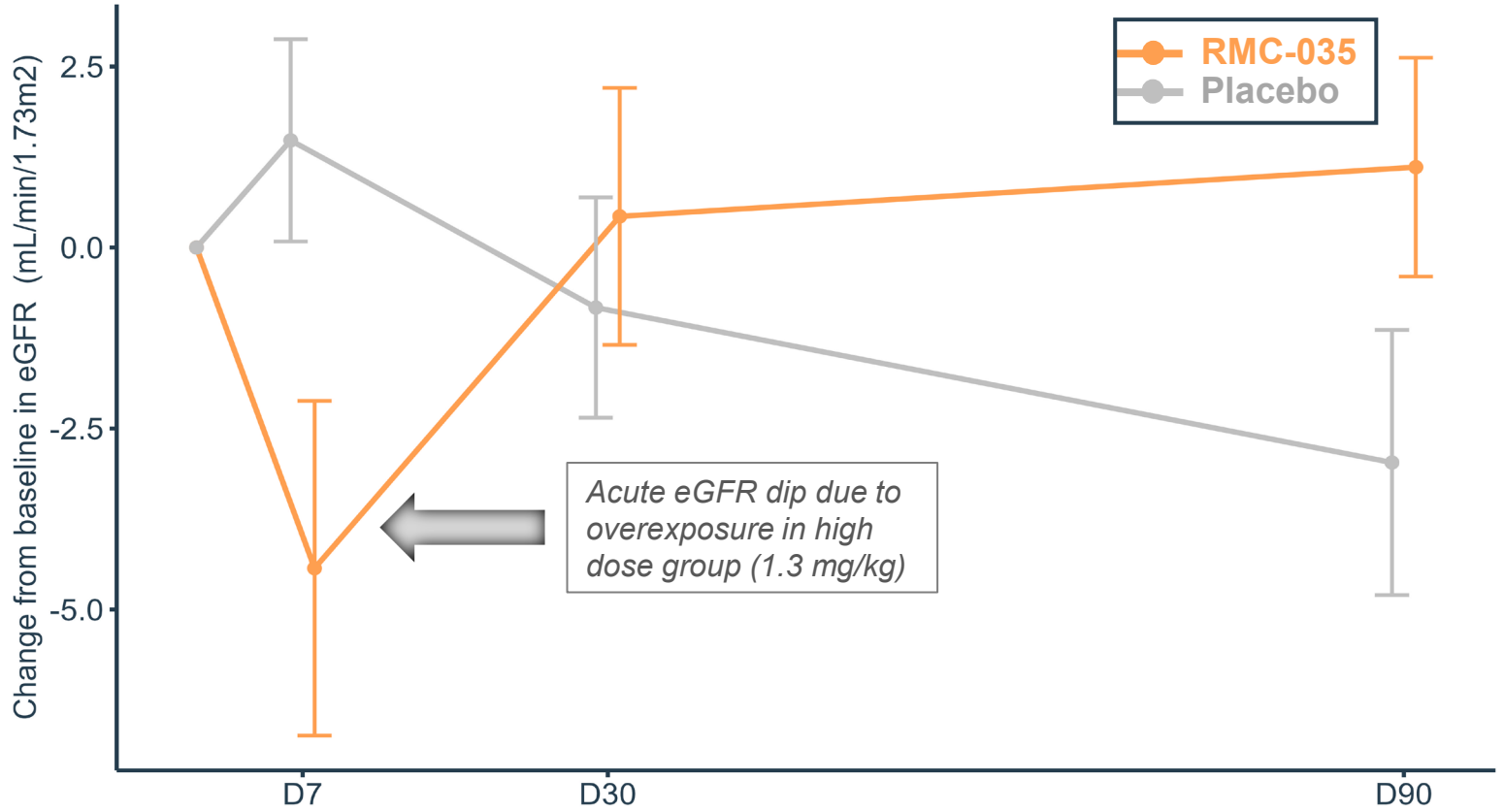
- **Statistically significant & clinically relevant improvement of renal function (eGFR) vs placebo**
  - Improved eGFR vs placebo 4.3 mL/min (full population)
  - Improved eGFR vs placebo 7.9 mL/min (pre-defined subgroup of patients with chronic kidney disease [CKD])
- **Reduced proportion of patients with MAKE (i.e., severe loss of kidney function)**
  - 59% risk reduction vs placebo for composite endpoint MAKE (death, dialysis or ≥ 25% eGFR loss)
  - FDA recommends **MAKE as primary endpoint in Phase 3 – 20% risk reduction sufficient for approval**

Results support progression to Phase 2b

Study ROS-05 Clinical Study Report: Zarbock et al., eClinical Medicine 2024. eGFR, estimated glomerular filtration rate.

RENAL FUNCTION (EGFR) – CHANGE FROM BASELINE

Clinically & statistically significant Improvement of long-term renal function with RMC-035 vs placebo



	D7	D30	D90
RMC-035 (n)	77	68	64
Placebo (n)	73	69	69

eGFR benefit at Day 90:

MMRM model
4.3 mL/min **p=0.06***

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

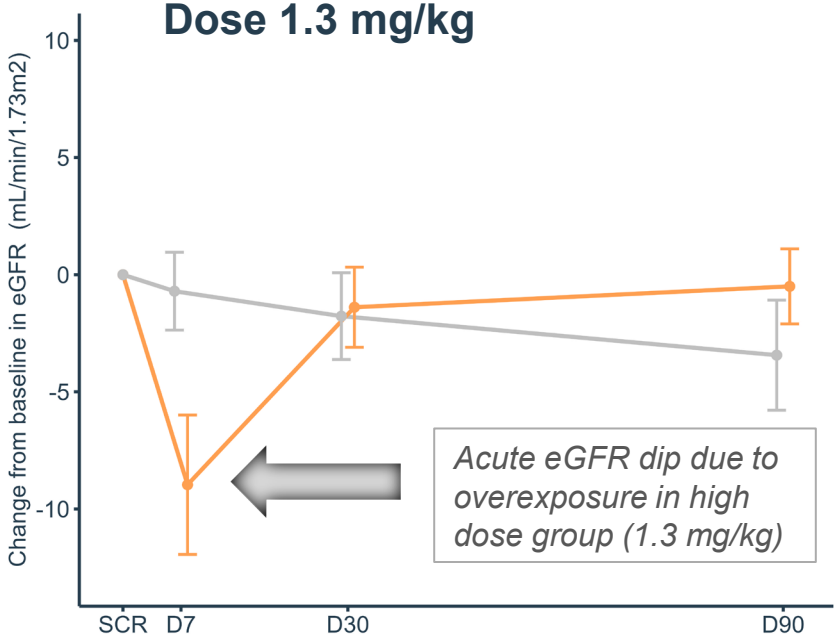
Source: Table 14.2.3.3.1. Error bars indicate mean +/- Standard Error (SE); eGFR, estimated glomerular filtration rate; MMRM, Mixed Model of Repeated Measures.

RENAL FUNCTION (EGFR) – CHANGE FROM BASELINE

Clinically & statistically significant Improvement of long-term renal function with RMC-035 vs placebo

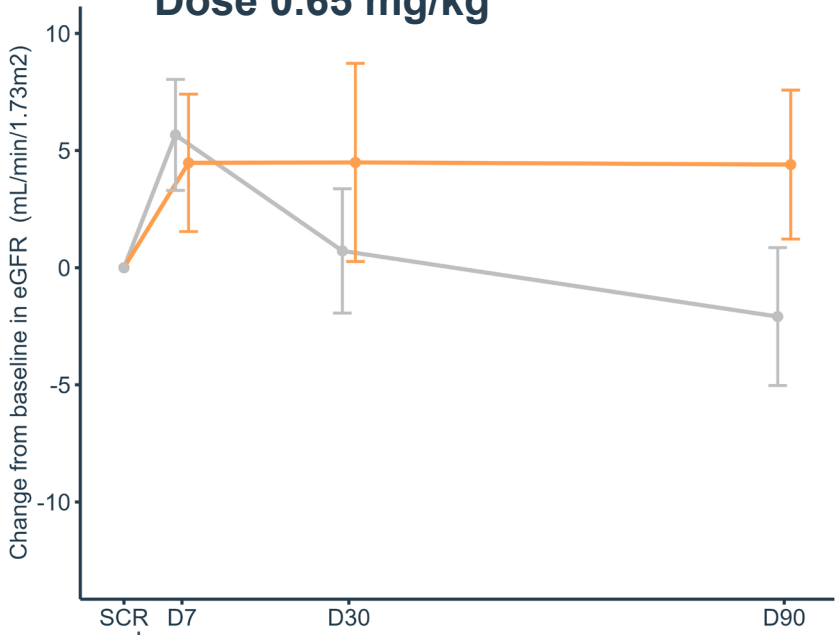
eGFR subgroups pre-specified based on different start doses and risk for kidney injury

eGFR ≥ 60 mL/min/1.73m^2
Dose 1.3 mg/kg



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

eGFR < 60 mL/min/1.73m^2
Dose 0.65 mg/kg



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

eGFR benefit at Day 90:

Subgroup	MMRM model
eGFR ≥ 60	2.3 mL/min p=0.41
eGFR < 60	7.9 mL/min **p=0.05**

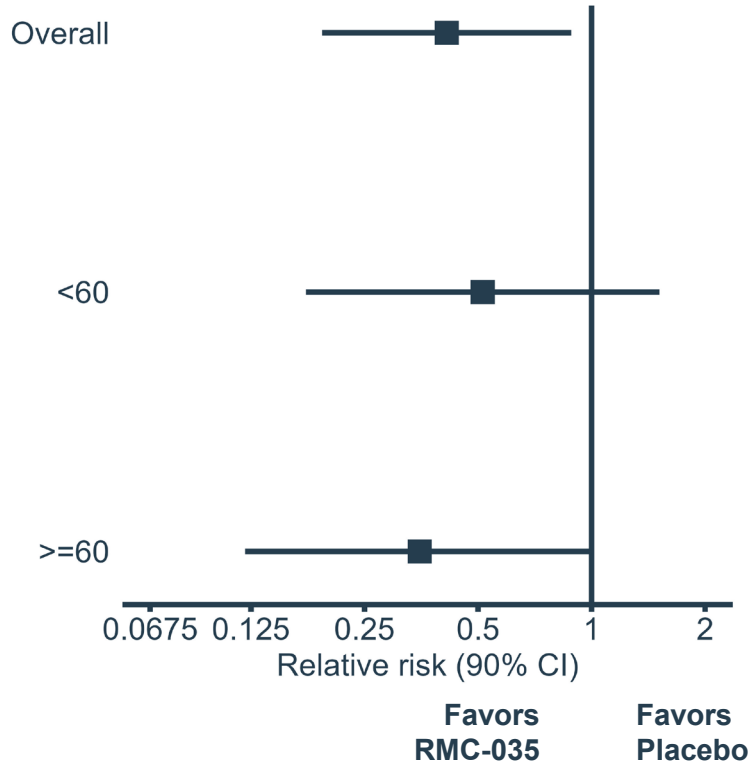
Pre-defined alpha level was 0.1.
P-values < 0.1 are statistically significant.

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

MAKE90* – REGULATORY PHASE 3 ENDPOINT MET

Clinically & statistically significant reduction of MAKE90 – efficacy signal present irrespective of start dose

	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<0.05**	

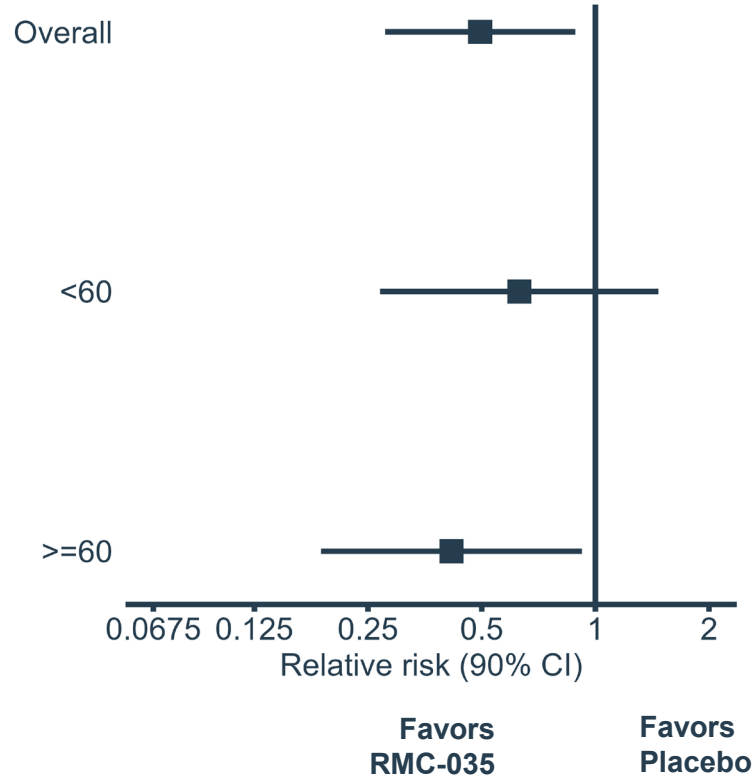


Source: Table 14.2.3.9.1. CI, confidence interval: MAKE, Major Adverse Kidney Events.
Note (*): eGFR calculated using CKD-EPI equation with serum creatinine.

SENSITIVITY ANALYSIS OF MAKE90*

Confirms efficacy signal on regulatory phase 3 endpoint – irrespective of start dose

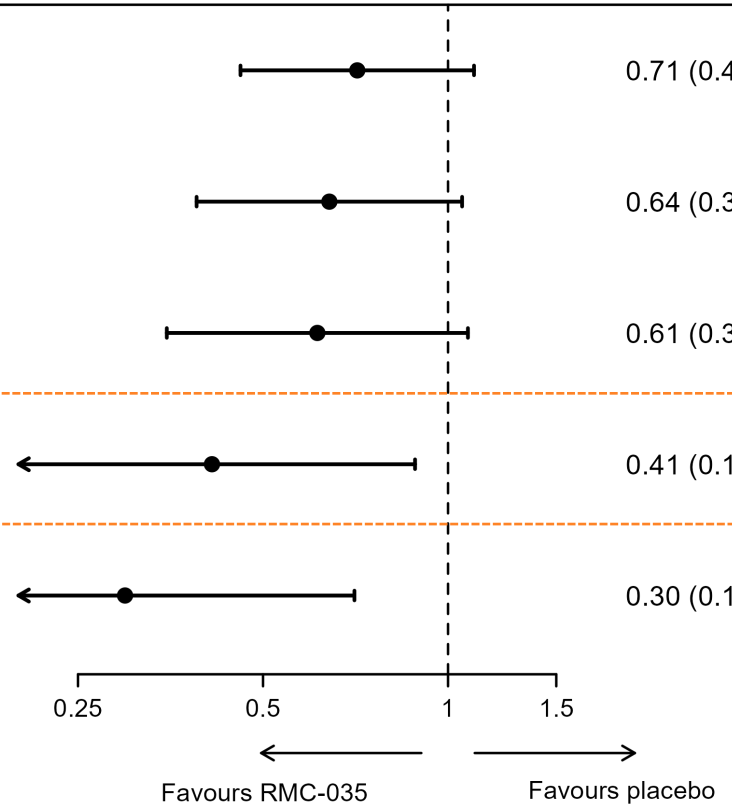
	RMC-035 (N=89)	Placebo (N=88)
Number (%) of Subjects with MAKE at Day 90	10 (11.2%)	20 (22.7%)
Death through Day 90	4	4
Dialysis through Day 90	3	2
≥25% eGFR* reduction at Day 90	**7**	**15**
Relative Risk (90% CI)	0.50 (0.28, 0.88) **p<0.05**	



Source: Table 14.2.3.9.3. CI, confidence interval: MAKE, Major Adverse Kidney Events.
Note (*): eGFR calculated using CKD-EPI equation with serum creatinine & cystatin C

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



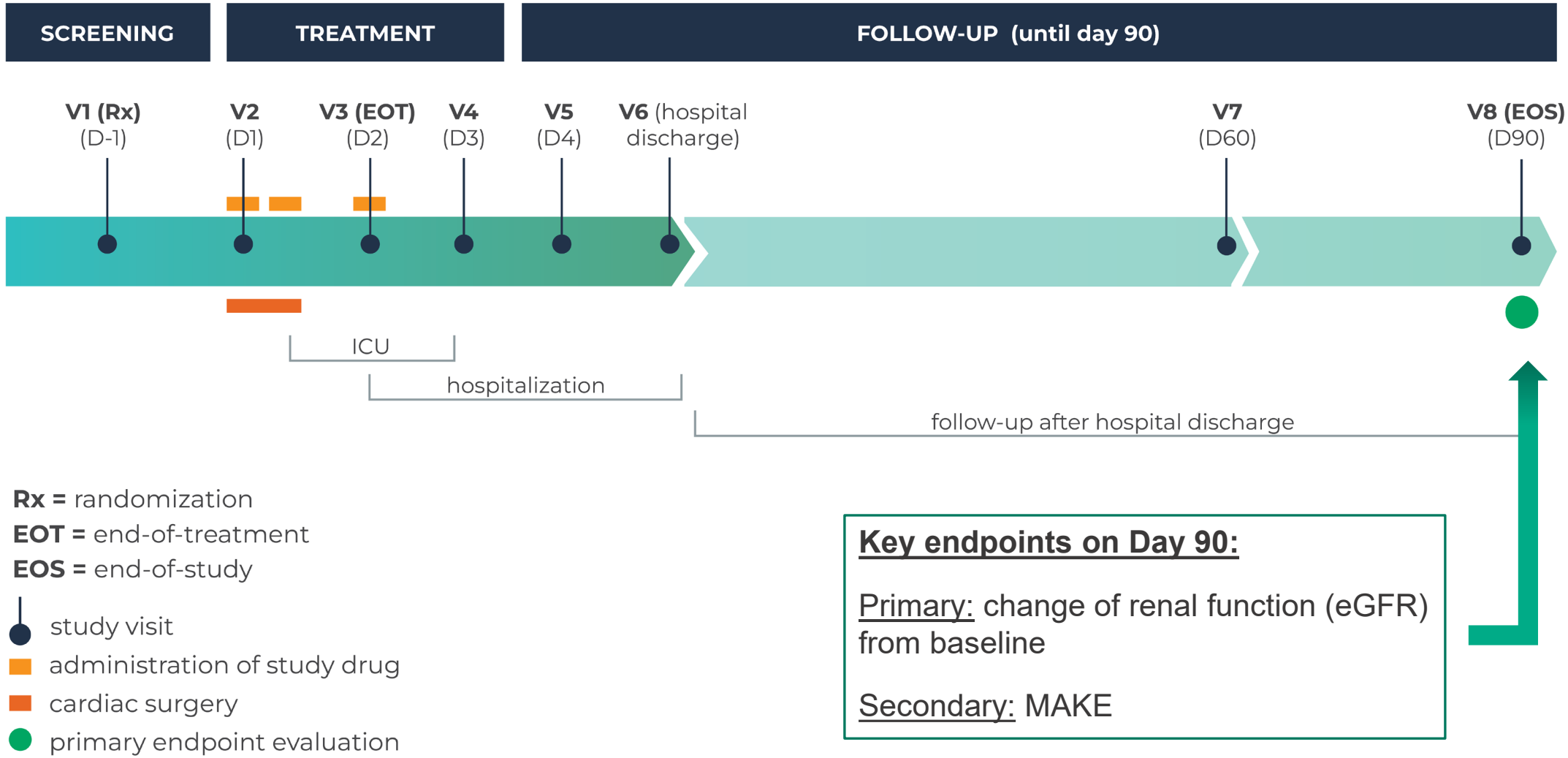
Source: post-hoc analyses of Study 21-ROS-05. MAKE, major adverse kidney events; eGFR, estimated glomerular filtration rate

ONGOING PHASE 2b *POINTER* STUDY – OUTLINE & OBJECTIVES

- Study protocol **reviewed by the FDA** (US IND study)
- **First patient enrolled in Q3 2024** (Canada & EU)
- Main objective: **establish dose & target population** for Phase 3
- Sample size **~160 patients** (30% required to have chronic kidney disease [CKD])
- Two dose arms (60 & 30 mg) & Placebo (2:2:3 randomization)
- **Data Safety Monitoring Committee** (DSMC) to review data from 1/3 & 2/3 of patients
- Expected **recruitment time ~1 year**
- All patients **followed up to 90 days after surgery**

IND, investigational new drug

ONGOING PHASE 2b *POINTER* STUDY – FLOWCHART



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

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

Key endpoints on Day 90:

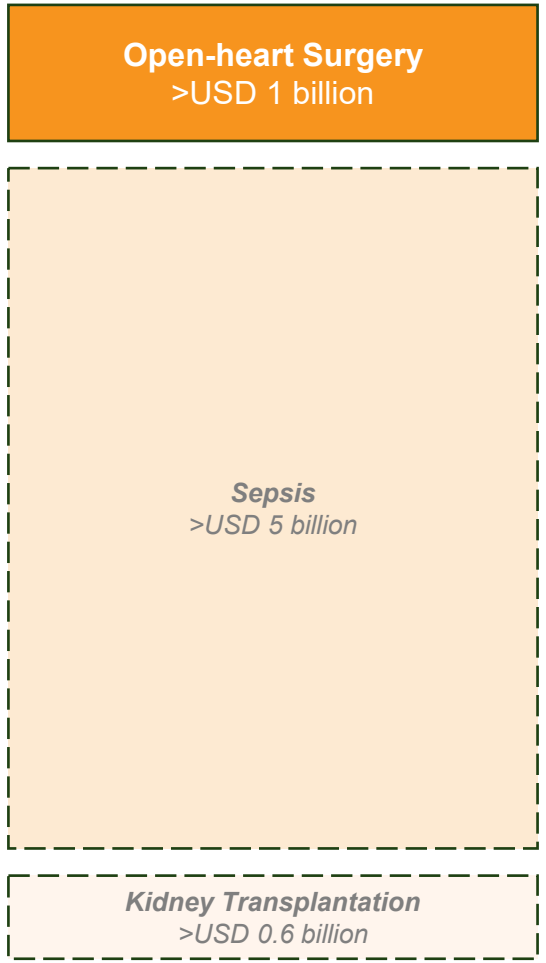
Primary: change of renal function (eGFR) from baseline

Secondary: MAKE

ICU, intensive care unit; eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney outcomes

CLEAR PATH TOWARDS MARKET APPROVAL FOR RMC-035

- **Fast Track Designation** granted by the US FDA
  - *Reducing risk for death, dialysis or irreversible loss of kidney function in patients undergoing open-chest cardiac surgery at high risk for acute kidney injury*
- Indication eligible for **Breakthrough Therapy Designation**
- **Single pivotal Phase 3 study** sufficient to support market approval
  - *Primary endpoint MAKE at Day 90 after surgery (~600 patients)*
  - *Potential for accelerated approval based on interim analysis of eGFR (~300 patients)*
  - *First-to-market potential*
- **Phase 3 Expansion Opportunities**
  - ***Sepsis*** *Phase 3 ready and* ***Kidney Transplant*** *Phase 2a/b ready, following successful Phase 2b POINTER results*



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), HCUP 2019, J Thorac Dis. 2018 Mar; 10(3): 1960–1967, Pickering JW et al. Am J Kidney Dis. 2015. eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney events

STRONG VALUE PROPOSITION – EFFICACY & COST-BENEFIT PROFILE

Robust kidney protection in AKITA study

- *~5 x greater eGFR effect than one year of standard-of-care CKD treatment*
- *3 x greater risk reduction of MAKE than required for FDA approval*

Strong evidence for eGFR in Cost Effectiveness Models

- *Value dossier supported by available health economic data in patients with CKD*

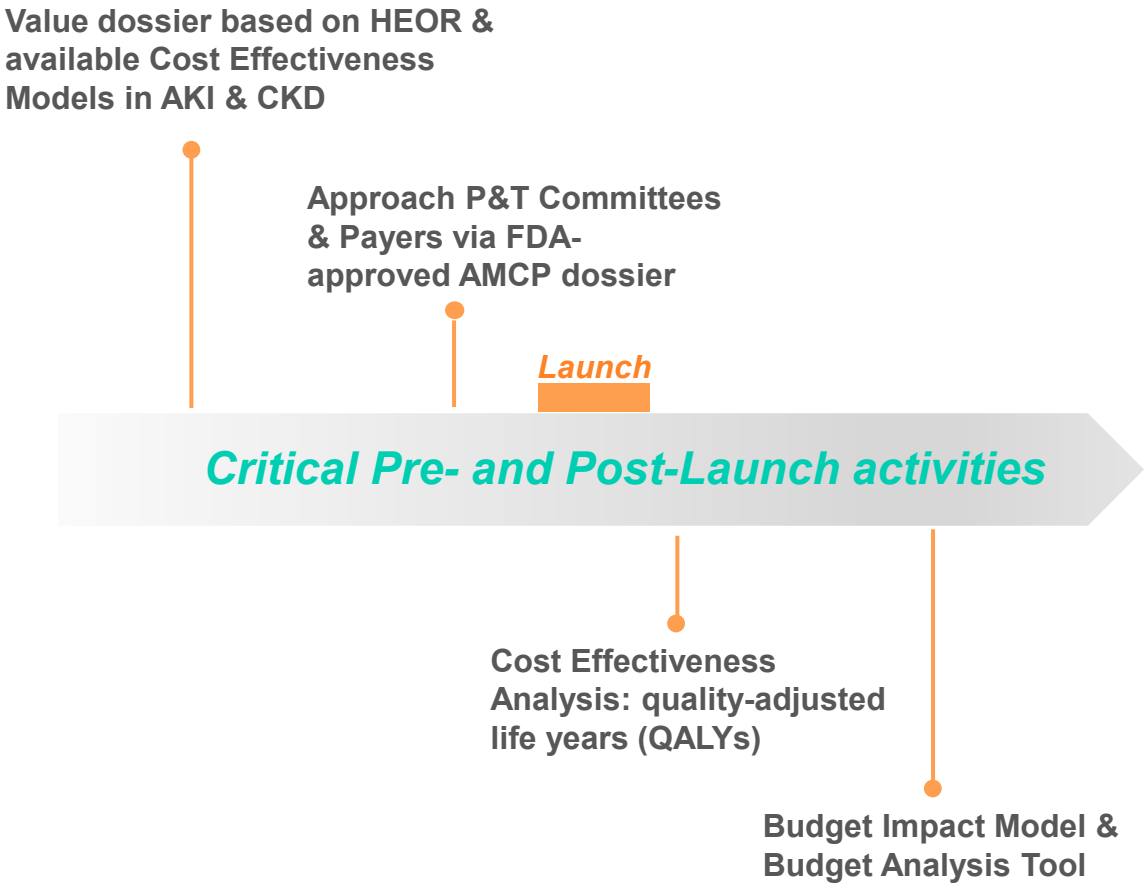
Short-term therapeutic benefit

(AKI, dialysis, length of hospital stay & re-admission)

- *Acute benefits offer direct & indirect hospital savings*

Attractive cost-benefit profile

- *Anticipated formulary inclusion with marginal impact on hospital cost*
- *Fulfils NTAP criteria*



eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; MAKE, major adverse kidney events; AKI, acute kidney injury; ICU, intensive care unit; AMCP; academy of managed care pharmacy; NTAP, new technology add-on payment

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

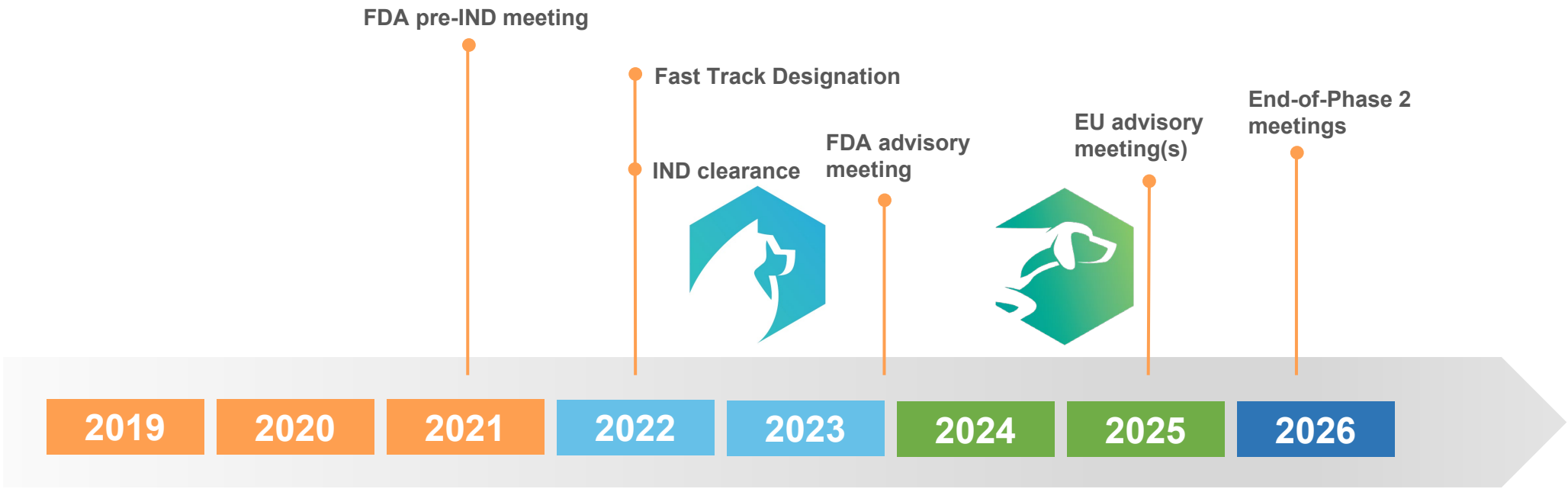
COMPANY (DRUG)	PHASE	MODE OF ACTION	POC DATA HEART SURGERY	COMMENT
Guard Therapeutics (RMC-035)	**2b**	**A1M analog**	**Yes**	Study ongoing, enrolment target 161 patients. Enrollment initiated in Canada in August/September 2024. Recruitment in EU set to begin October 2024. All regulatory and ethics approvals are in place. Top-line results expected year-end 2025. Efficacy demonstrated with RMC-035 vs placebo on eGFR & MAKE90 endpoints in Phase 2a AKITA study.
Novartis (TIN-816)	2a	Human CD39 enzyme	-	Study ongoing, enrollment target 120 patients. Recruitment delayed; results projected for September 2025. No efficacy data available based on Phase 1 program.
AstraZeneca / Alexion (Ultomiris)	3	Complement 5 inhibitor	-	No efficacy data in open-heart surgery. Drug already approved for Paroxysmal Nocturnal Hemoglobinuria (PNH) and atypical Hemolytic Uremic Syndrome (aHUS); Pivotal study in open-heart surgery started in Q3 2023.
Renibus Therapeutics (RBT-1)	3	Iron sucrose + stannus protoporhyrin	-	Drug targets acute endpoints like length of hospital stay & hospital re-admission rate. Did not show efficacy on renal endpoints in Phase 2a study.

RECENT PHARMA DEALS IN NEPHROLOGY
– TOTAL DEAL VALUE OVER $11BN 2023-24 YTD

TARGET	ACQUIRER	YEAR	DEAL VALUE	STAGE	LEAD ASSET	INDICATION
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

IgAN, IgA nephropathy; CKD, chronic kidney disease; ESRD, end-stage renal disease; NDA, new drug application

KEY MILESTONES & DELIVERY ACCORDING TO 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

Optional Phase 2a/b study in kidney transplantation

Additional opportunities

with RMC-035 & GTX peptides (modified peptides derived from A1M)

ADDITIONAL OPPORTUNITY FOR RMC-035 – SEPSIS

- Sepsis is **leading cause of acute kidney injury (AKI)**. Multifactorial etiology, kidney cell stress due to reduced perfusion, oxidative stress, endotoxins and inflammation
- **RMC-035 efficacious in preclinical sepsis models**
- In the US, **~1.7 million** patients develop sepsis each year**; ~800,000 patients** with sepsis develop AKI; and **~250,000 patients** develop CKD
- Dosing regimen: once daily up to 5 days; First dose given at sepsis diagnosis (ICU admission)
- Clear regulatory path to market approval – **Major Adverse Kidney Events (MAKE) at 90 days**
- **Single confirmatory Phase 3 study** sufficient for approval
  - *Sample size ~400-600 patients depending on eligibility criteria*
  - *Recruitment time ~2 years*
- **Pivotal Phase 3 study in sepsis enabled by Phase 2b POINTER study (heart surgery)**
  - *Interim analysis with sample size re-estimation to be built in in the absence of preceding efficacy study*
  - *Should be preceded by a Phase 1b study of approximately 15-20 patients to evaluate exposure & safety*

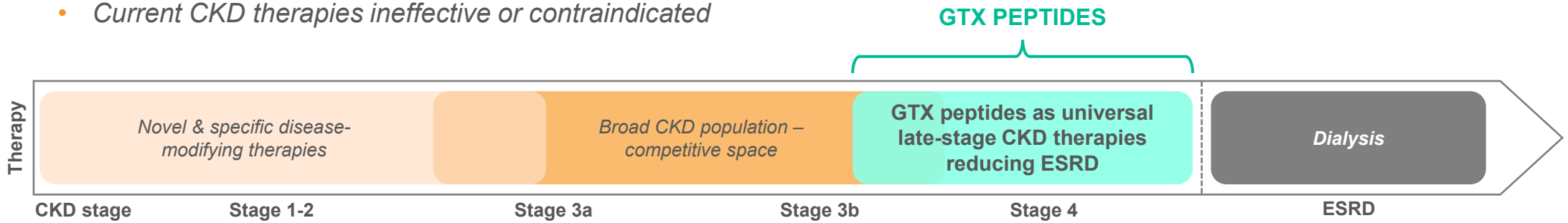
ADDITIONAL OPPORTUNITY FOR RMC-035 – KIDNEY TRANSPLANTATION

- **Phase 1b study of RMC-035 completed**
- Acute kidney graft dysfunction & impaired long-term dysfunction in deceased donor transplantation due to **graft ischemia & ischemia-reperfusion injury,** and **inflammatory / fibrotic response**
- Approximately **20,000 deceased donor kidney transplantation** performed annually in US – eligible for **orphan drug designation**
- Treatment goal: **protect long-term graft function in recipient**, avoiding need for re-transplantation
- Dosing regimen: once daily up to 5 days; First dose given intra-operatively to graft recipient
- **Clear regulatory path** to market approval – **eGFR at 1 year** after transplantation
- **Single confirmatory Phase 3 study** sufficient for approval
  - *Sample size 300-600 patients depending on eligibility criteria*
  - *Recruitment time 2-3 years*
- New formulation considered, may enable higher price point than in open-heart surgery

eGFR, estimated glomerular filtration rate.

GTX PEPTIDES (A1M-DERIVED) – MASSIVE OPPORTUNITY IN LATE-STAGE CKD

- **GTX peptides: Subcutaneous delivery, chronic treatment for late-stage CKD**
- **High potency and efficacy, comparable to RMC-035**
- **Initially targeting late-stage CKD patients:**
  - *Highest risk for progression to ESRD*
  - *Often excluded from clinical trials*
  - *Current CKD therapies ineffective or contraindicated*



- **Broad impact across CKD etiologies, including orphan diseases**
  - *Demonstrated robust efficacy in a wide range of disease models*
- Ready for candidate nomination – approximately 2 years from IND

CKD, chronic kidney disease; ESRD, end-stage renal disease.
CKD classification based on Kidney Disease Improving Global Outcomes (KDIGO)

PIONEERING TRANSFORMATIVE MEDICINES FOR KIDNEY DISEASE

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- **Clinical proof-of-concept established in Phase 2a AKITA study with 177 patients**
  - **59% reduction vs placebo (MAKE, regulatory endpoint)**
- **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 programme** and **Phase 2a/b ready kidney transplantation programme** for >USD 5.6 billion market
- **Unique positioning of preclinical GTX peptides** in late stage and orphan chronic kidney diseases for >USD 8 billion market
- Listed in Stockholm with top shareholders including Industrifonden and Swedbank Robur [Nasdaq FN Growth Market: GUARD]

GUARD THERAPEUTICS