GUARD THERAPEUTICS

Capital Markets Day

Stockholm, Sweden

21 September 2022

WELCOME & INTRODUCTION

TOBIAS AGERVALD, CHIEF EXECUTIVE OFFICER

GUARD THERAPEUTICS INTERNATIONAL AB

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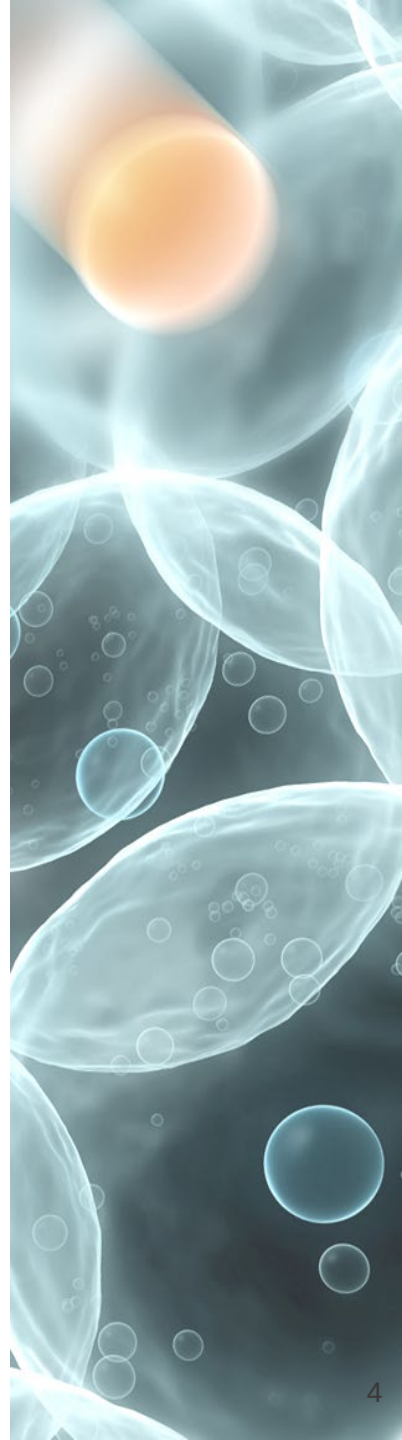
GUARD THERAPEUTICS AT A GLANCE

- Developing targeted therapies for Acute Kidney Injuries (AKI) – clinical stage company since 2019
- Lead investigational drug RMC-035 (ROSgard)
- Robust preclinical program with efficacy data in >10 disease models
- Clinical Phase 1 program including 4 studies
- Recently initiated large global Phase 2 study for the treatment of Cardiac Surgery associated AKI (CS-AKI)
- CS-AKI a USD >1bn opportunity with no approved therapies
- Recently initiated second clinical program in kidney transplantation
- Listed on Nasdaq First North Growth Market in Stockholm [GUARD] with SEK ~325m market cap (~USD 31m) & SEK 151m in cash (June 31, 2022)



GUEST SPEAKER – PROF ALEXANDER ZARBOCK, MD

- Professor of anesthesiology and intensive care, University of Münster, Germany
- Director of Anesthesiology, Operative Intensive Care and Pain Therapy, Münster University Hospital
- Global Key Opinion Leader in the field of Acute Kidney Injury (AKI)
- Main academic interest include AKI, sepsis and organ protection
- Author of more than 150 scientific articles and book chapters in this field
- Principal Investigator for the ongoing Phase 2 study (AKITA)

SPEAKERS FROM GUARD THERAPEUTICS

NAME / POSITION	EXPERIENCE	
 **TOBIAS L. AGERVALD** MD, PhD, CEO	**+10** years in industry	astellas
 **MICHAEL REUSCH** MD, CMO	**+30** years in industry	Fujisawa astellas
 **PETER GILMOUR** MSc, PhD, CSO/Head of Preclinical	**+20** years in industry	AstraZeneca astellas

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AGENDA

- **Acute kidney injury in cardiac surgery – an intensive care physician's perspective**
  - Professor Alexander Zarbock, MD
- **RMC-035 – a novel first-in-class investigational drug**
  - Peter Gilmour, PhD, Chief Scientific Officer/Head of Preclinical Sciences
- **Clinical experience of RMC-035 – overview of Phase 1 program & Phase 2 AKITA study**
  - Dr Michael Reusch, Chief Medical Officer
- **Coffee break**
- **Clinical strategy for RMC-035 in kidney transplantation**
  - Dr Michael Reusch, Chief Medical Officer
- **Market considerations & future pricing/reimbursement opportunities**
  - Tobias Agervald, Chief Executive Officer
- **Summary**
  - Tobias Agervald, Chief Executive Officer
- **Q&A**

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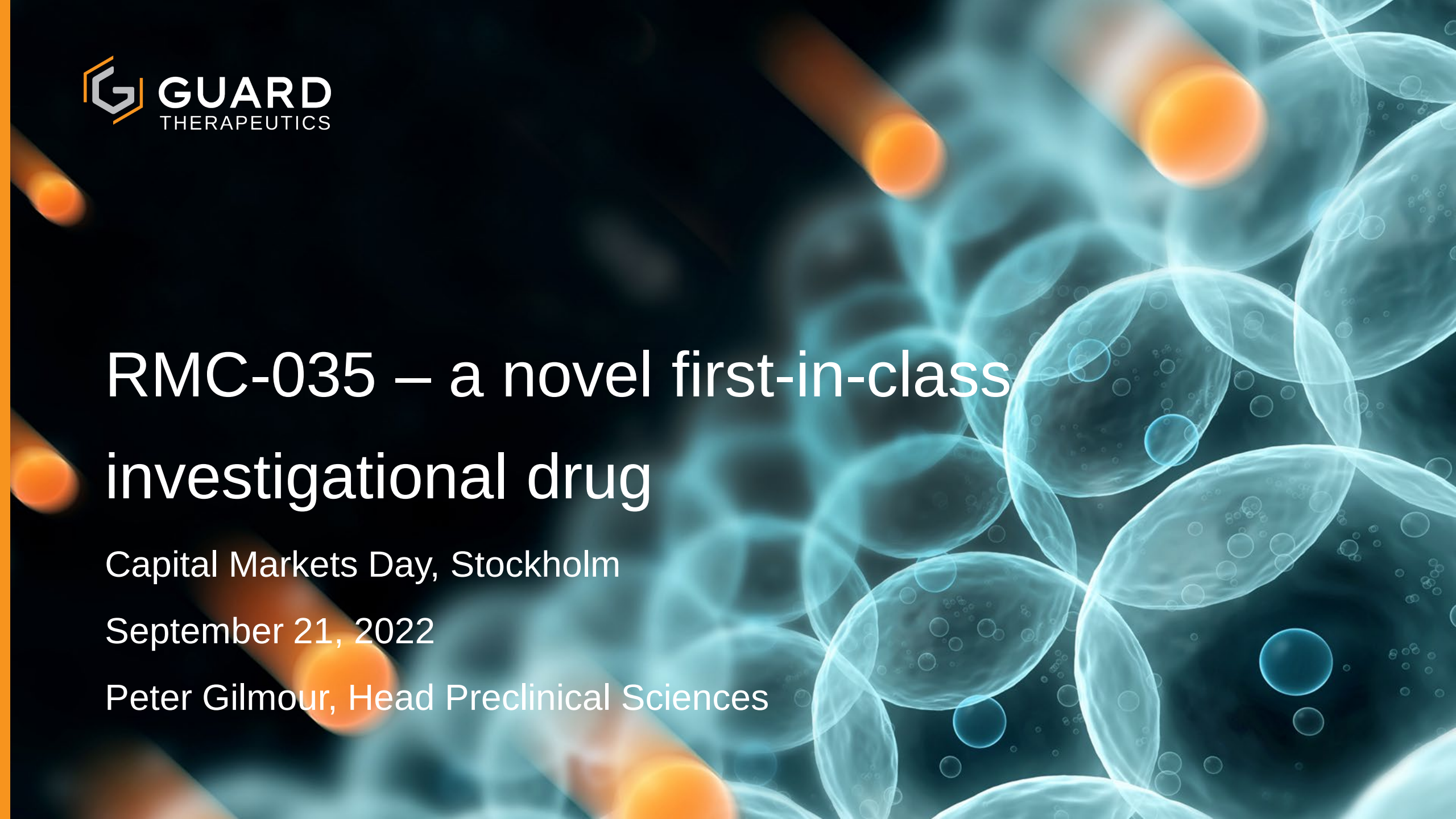

RMC-035 – a novel first-in-class investigational drug

Capital Markets Day, Stockholm

September 21, 2022

Peter Gilmour, Head Preclinical Sciences

RMC-035: FIRST-IN-CLASS INVESTIGATIONAL DRUG

- RMC-035 (ROSgard) is a first-in-class drug developed for the treatment of acute kidney injuries (AKI)
- Biological – delivered via intravenous infusion
  - Recombinant variant of the endogenous protein alpha-1-microglobulin (A1M)
- Short treatment duration (2–5 days)
- Preclinical efficacy shown in >10 disease models
- Ideal for treatment of AKI
  - Mechanism of action well aligned with disease pathways
  - Targets several pathways – differentiation from other candidate therapies
  - Ideal biodistribution with rapid uptake in kidney (tubular) cells – the principal site of cellular injury in AKI

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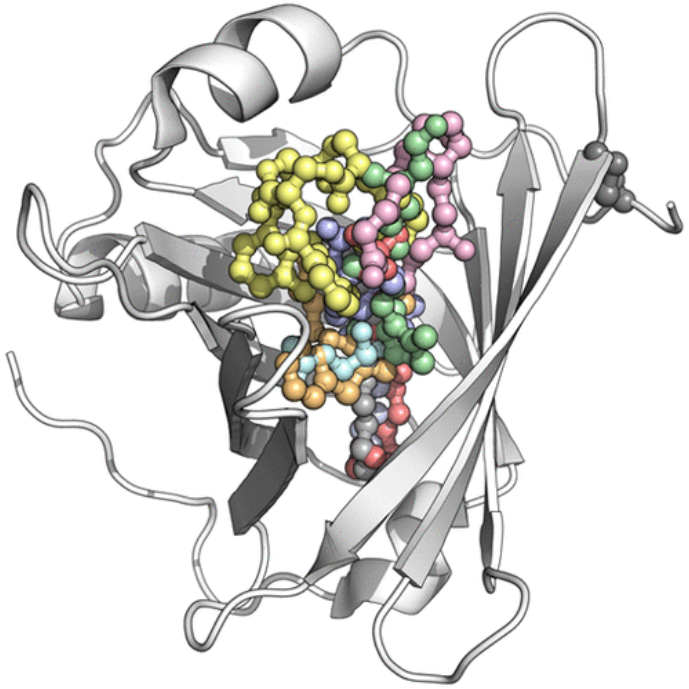
LIPOCALINS – A BLUEPRINT FOR NOVEL DRUGS

- Highly conserved protein superfamily, found in bacteria, plants and vertebrates
- Barrel shaped 3-dimensional structures, with protein strands forming a cylinder, containing internal ligand binding sites
- Involved in binding, storage and transportation of small hydrophobic or chemically reactive molecules
  - Steroids, lipids and heme
  - Can act as immune modulators, antioxidants, signal transducers, tissue development and cell homeostasis



Flower (1996) Biochem. J. 318:1-14

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ALPHA 1-MICROGLOBULIN – A NATURAL PROTECTOR OF THE KIDNEYS

- Evolutionary conserved, found in all vertebrates
- Mainly produced in the liver
  - Expression is stimulated by oxidative stress and free heme
- Plasma and tissue distribution
  - Present in blood, extravascular compartments and all tissues
  - Renal clearance
- Serves as a tissue housekeeping protein (‘circulating wastebasket’)
- Biochemical structure facilitates multiple mechanisms of action

Properties of endogenous A1M protein can be leveraged for the treatment of AKI

Bergwik et al (2021) Front. Physiol. 12:645650.

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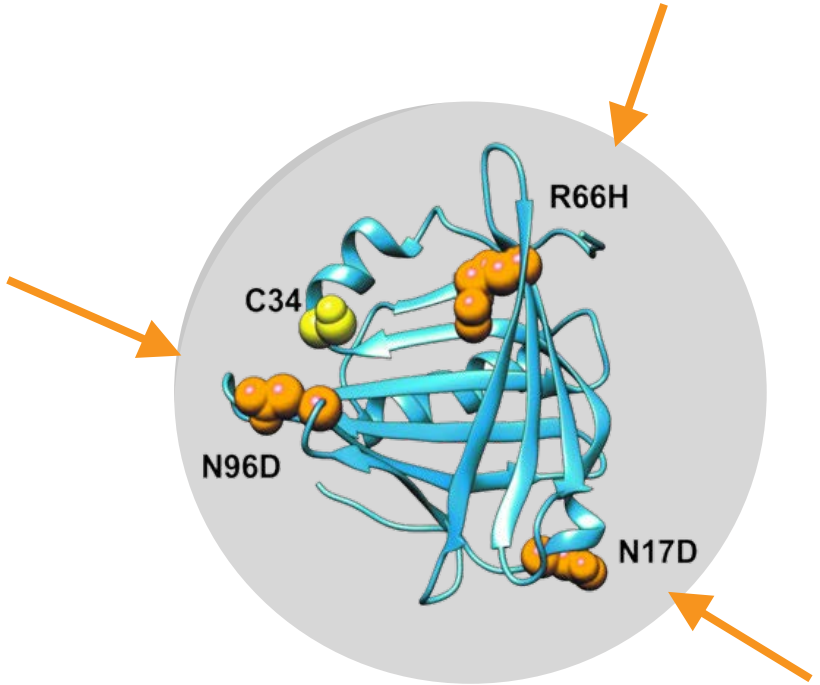
RMC-035 IS A FIRST-IN-CLASS DRUG BASED ON ALPHA 1-MICROGLOBULIN STRUCTURE

- RMC-035 is a druggable, recombinant and patent protected variant of the endogenous protein
- Physicochemical changes compared to native protein:
  - Three amino acid substitutions to improve solubility
  - N-terminal tag for increased stability & solubility
  - Lack of glycosylation (manufactured in E. coli)



RMC-035 has improved physicochemical properties with retained potency as compared to the endogenous A1M protein

Åkerström et al. Antiox Redox Signal (2019) 30(4):489

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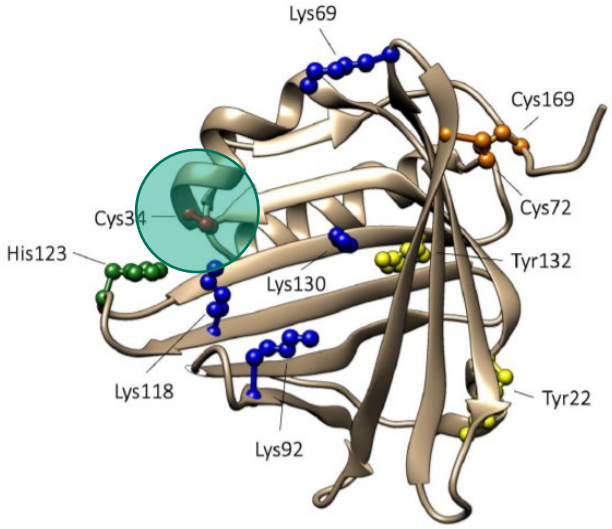
RMC-035 STRUCTURE-FUNCTION RELATIONSHIP ARE WELL CHARACTERIZED

1. **Reductase activity** – reduction of 5–6 free radicals per RMC-035 molecule
2. **Free radical trapping** – binds free radicals including reactive oxygen species
3. **Heme binding & degradation** – two specific heme-binding sites
4. **Mitochondrial binding/stabilization** – binds and stabilizes cytochrome C

- Cysteine and the three-dimensional protein structure provide the basis for specific protein functions



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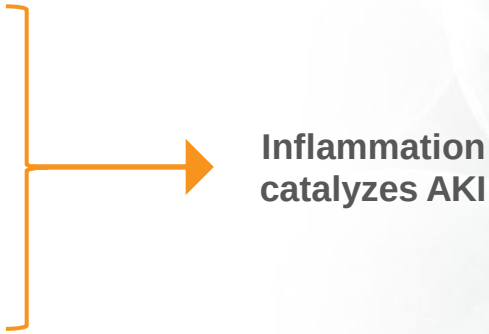
RMC-035 MECHANISMS TARGET KEY PATHWAYS IN CARDIAC SURGERY-ASSOCIATED (CS-AKI) AKI

- CS-AKI is mainly initiated by ischemic kidney injury and heme-driven toxicity
  - **Ischemia/hypoxia** during surgery
  - **Heme-injury** caused by hemolysis (release of heme from red blood cells during CPB)
- Downstream consequences of renal ischemia and hemolysis
  - Surge of toxic free radicals
  - Reduced reductase activity/capacity in tissue
  - Surge of circulating free heme
  - Mitochondrial dysfunction & renal tubular cell death



Inflammation catalyzes AKI

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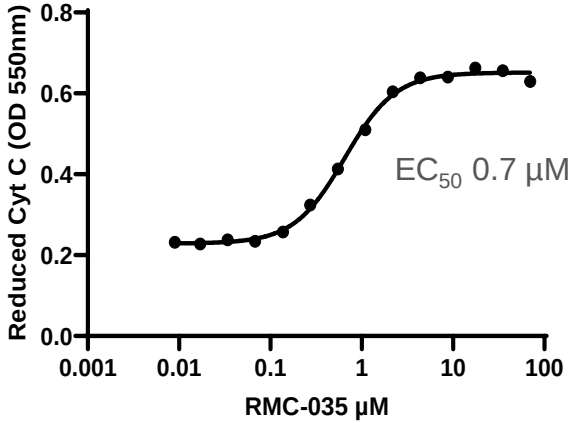
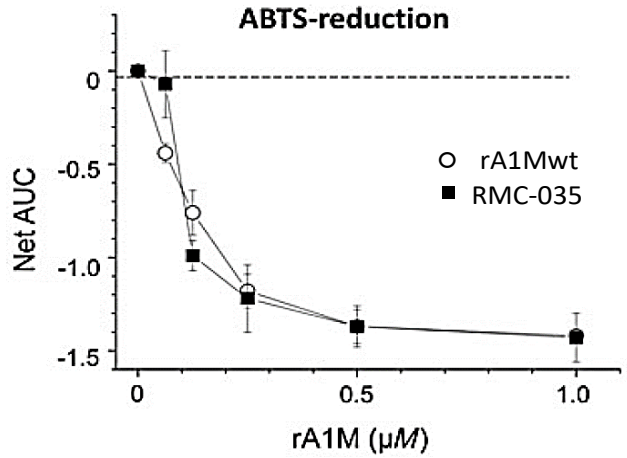
RMC-035 IS A POTENT REDUCING AGENT IN VITRO

- Oxidized molecules induce oxidative stress in kidneys during ischemia
- RMC-035 reduces oxidized Cytochrome C in a dose-dependent way
- RMC-035 reduces the synthetic free radical molecule ABTS in a dose-dependent manner as determined by ABTS abundance





Study report GTI-PHARM-001
Åkerström et al. (2019) Antiox Redox Signal 30(4): 489
ABTS -2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid; AUC - area under the curve; rA!M rA!M: recombinant human A1M

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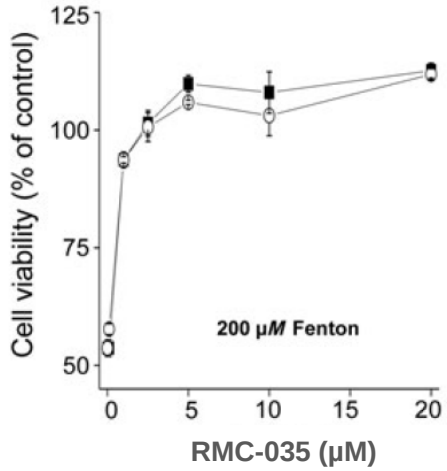
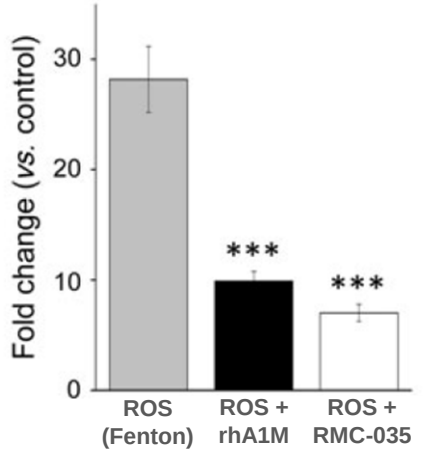
RMC-035 PROTECTS AGAINST CELL INJURY CAUSED BY OXIDATIVE STRESS

- Reactive oxygen species (ROS) damage human kidney cells
- RMC-035 scavenges Fenton chemistry-generated radicals (ROS)
- RMC-035 prevent human kidney (HK-2) cell death and reduce expression of the stress-response gene heme oxygenase-1 (HO-1)



RMC-035 (▪) & A1M (○) scavenge ROS and reduce HK-2 cell death in vitro



RMC-035 & A1M prevent ROS-induced expression of HO-1

*** p<0.001

Åkerström et al. (2019) Antiox Redox Signal 30(4): 489

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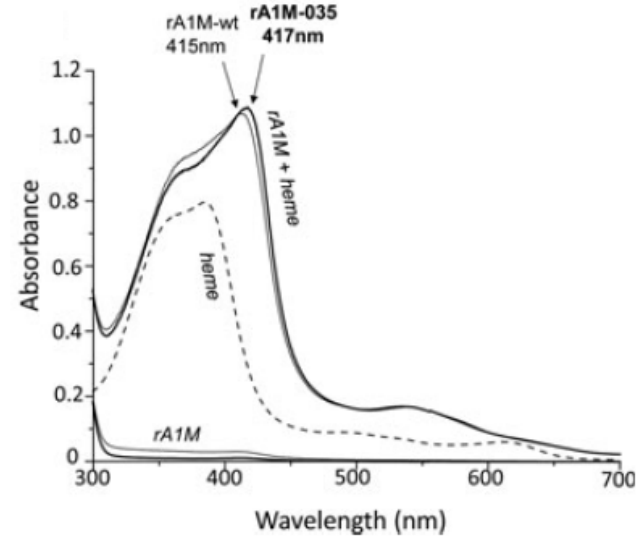
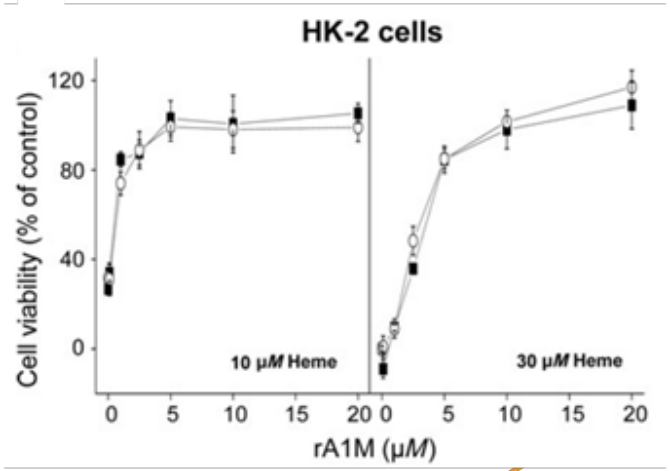
RMC-035 BINDS HEME & REDUCES HEME TOXICITY

- RMC-035 bind heme as evaluated by absorbance spectroscopy
  - ➢ RMC-035 retained heme-binding capacity as compared to native protein with similar absorbance spectra
- RMC-035 reduces heme-mediated kidney cell death in vitro





Rutardottir et al. Biochimica et Biophysical Acta (2016) 1864(1):29
Åkerström et al. Antiox Redox Signal (2019) 30(4):489
rA!M: recombinant human A1M

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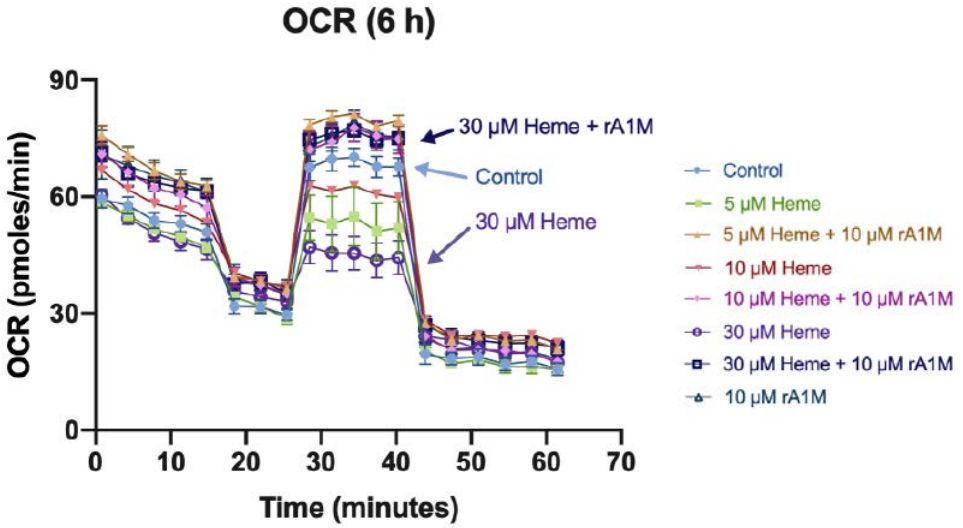
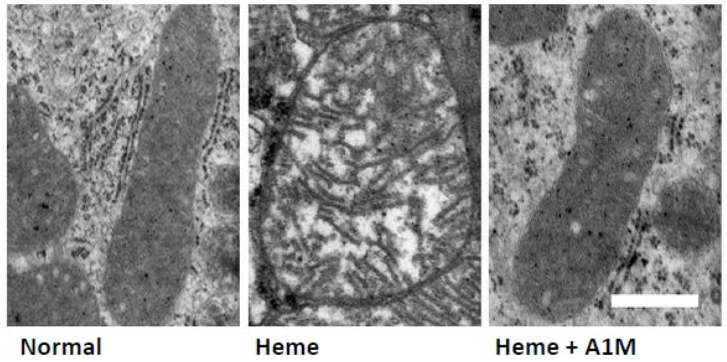
RMC-035 PROTECTS MITOCHONDRIAL FUNCTION FROM HEME TOXICITY

- RMC-035 (tool compound)
  - Binds to mitochondria (complex I)
  - Stabilizes structure and function
  - Reduces ROS release
- Heme reduces mitochondrial function in HK-2 cells in vitro as shown by assessment of mitochondrial respiration (oxygen consumption rate; OCR)
- RMC-035 (tool compound)
  - Prevents heme-driven reduction of mitochondrial OCR
  - Preserves mitochondrial function



Human keratinocytes loss of mitochondrial structure & swelling caused by heme is prevented by RMC-035



Olsson et al. (2013) Antiox Redox Signal 18:2013
Kristiansson et al. (2020) Int. J Mol. Sci. 21:5825

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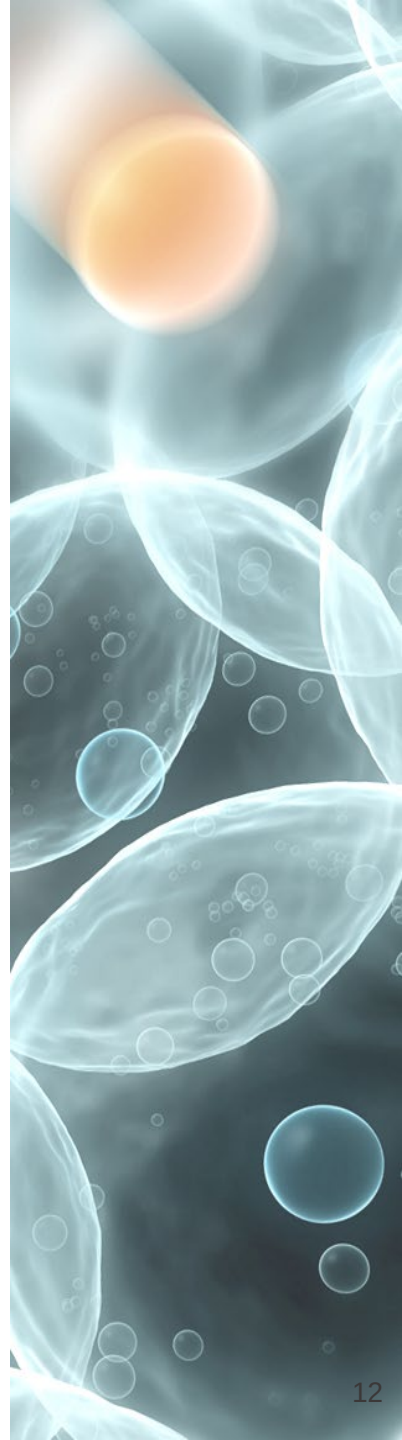
PHARMACOLOGY, PHARMACOKINETICS & TOXICOLOGY



ROBUST PHARMACOLOGY OF RMC-035 SUPPORTS POTENTIAL FOR CLINICAL TRANSLATION

- Consistent RMC-035 performance in vivo
  - Efficacy demonstrated in large number of disease models in multiple species
  - Protection in AKI and several non-kidney relevant disease models
- Optimal clinical posology for RMC-035 supported by in vivo pharmacology
  - Dose-finding
  - Frequency of dosing
  - Therapeutic vs preventive dosing
  - RMC-035 also effective in preventing AKI on top of existing kidney disease
- Upstream effect of RMC of initial kidney insult and pre-AKI initiation phase – not seen in previous AKI therapies
- Non-clinical pharmacology data supports translation into potential clinical efficacy

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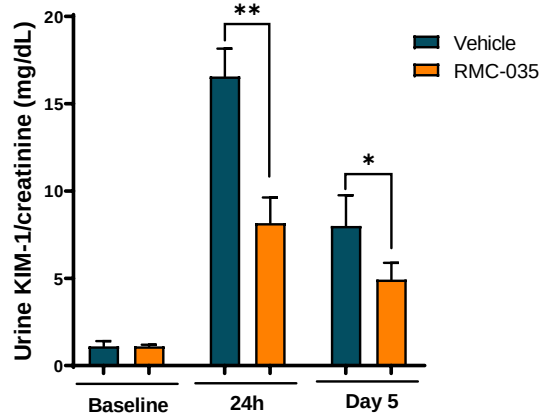
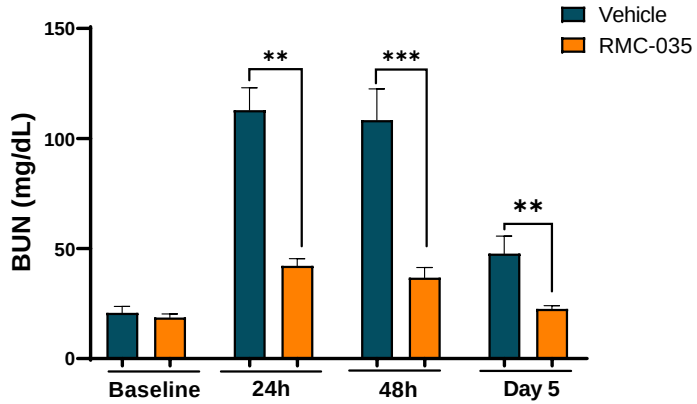
RMC-035 IS REDUCES KIDNEY TUBULAR CELL INJURY IN VIVO (RAT IRI-AKI MODEL)

- Rat kidney ischemia & reperfusion model of AKI
- RMC-035 administered IV at dose of 2 mg/kg
  - 5 x over 48h: matches clinical dosing schedule
- RMC-035 protects kidney from ischemic damage shown by translational markers of renal injury
  - Cell injury marker KIM-1 (kidney injury molecule-1)
  - BUN (Blood urea nitrogen)





* p<0.05
** p<0.01
*** p<0.001
n=6/7 per treatment group

Study report GTI-AKI-005

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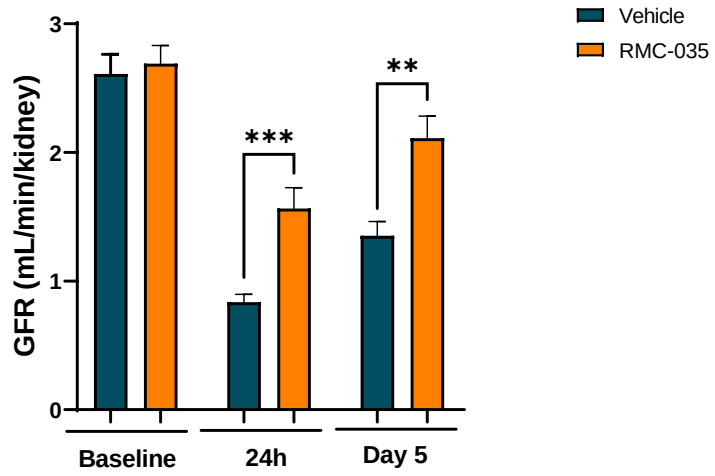
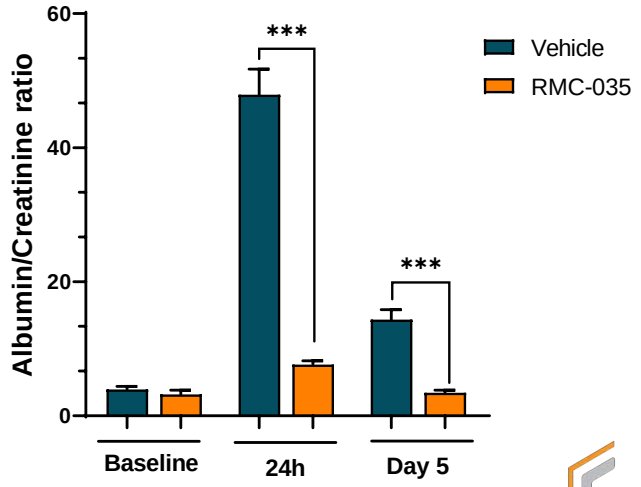
RMC-035 IMPROVES RENAL FUNCTION IN VIVO (RAT IRI-AKI MODEL)

- RMC-035 administered IV at 2 mg/kg
  - ➢ 5 x over 48h: matches clinical dosing schedule
- RMC-035 protects from loss of kidney renal function and damage
  - ➢ Improved glomerular filtration rate (GFR)
  - ➢ Reduced albuminuria (albumin/creatinine ratio)





** p<0.01
*** p<0.001
n=6/7 per treatment group

Study report GTI-AKI-005

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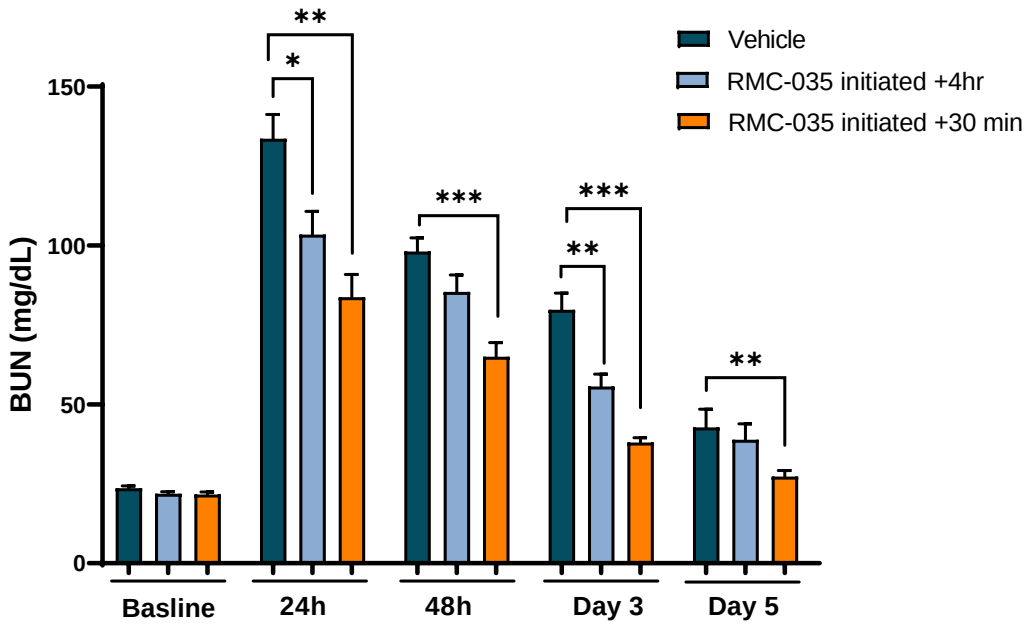
RMC-035 EFFECTIVE WITH THERAPEUTIC DOSING STRATEGY (RAT IRI-AKI MODEL)

- **Therapeutic dosing = dosing after onset of ischemia**
- Dosing in relation to initial ischemia evaluated:
  - 4 doses initiated at 4 hours post ischemia
  - 5 doses initiated at 0.5 hours post ischemia
- Therapeutic dosing reduces kidney function biomarker BUN
- Therapeutic dosing was effective, but best initiated soon after insult



* p<0.05
** p<0.01
*** p<0.001
n=7/8 per treatment group

Study report GTI-AKI-006

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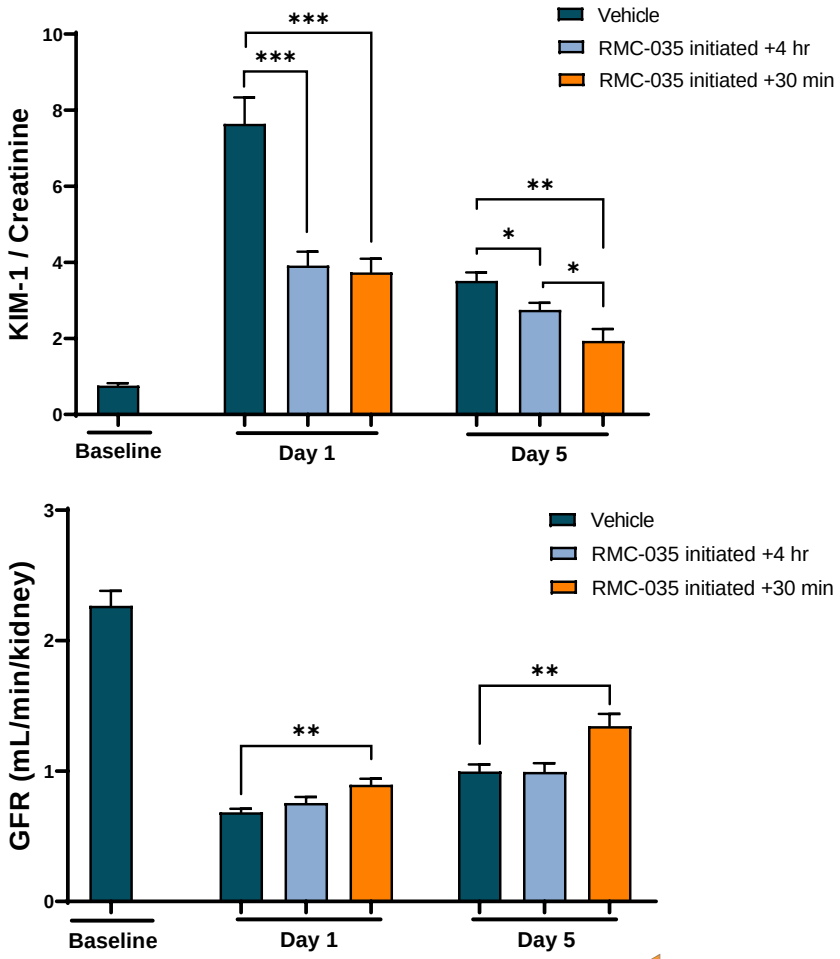
RMC-035 EFFECTIVE WITH THERAPEUTIC DOSING STRATEGY (RAT IRI-AKI MODEL)

- Therapeutic dosing = dosing after onset of ischemia
- Dosing in relation to initial ischemia evaluated:
  - 4 doses initiated at 4 hours post ischemia
  - 5 doses initiated at 0.5 hours post ischemia
- Therapeutic dosing reduces kidney injury biomarker KIM-1 and preserves renal function (GFR)
- Therapeutic dosing was effective, but best initiated soon after insult



*p<0.05
** p<0.01
*** p<0.001
n=7/8 per treatment group

Study report GTI-AKI-006

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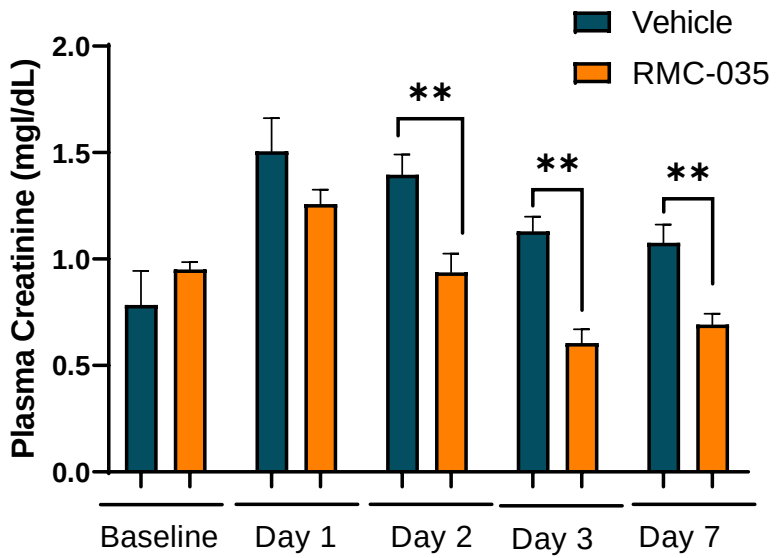
RMC-035 REDUCES AKI ON TOP OF EXISTING RENAL IMPAIRMENT (RAT 'AKI-ON-CKD MODEL')

- Removal of one kidney & remaining kidney subject to 30 min ischemia with 4-week recovery period
  - ➢ New ischemic injury to remaining kidney at 4 weeks
- RMC-035 administered IV at 2 mg/kg (per dose administration)
- 2 doses administered at 30 min before ischemia & 4 hours post-reperfusion
- RMC-035 was effective for reducing AKI on top of existing CKD as measured by renal function markers plasma creatinine & BUN



** p<0.01
*** p<0.001
n=5/6 per treatment group

Study report GTI-AKI-002

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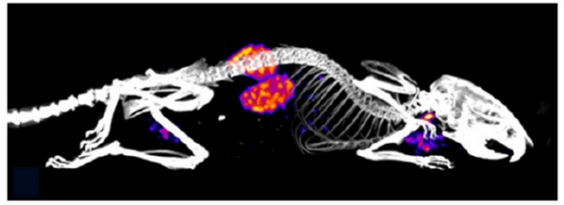
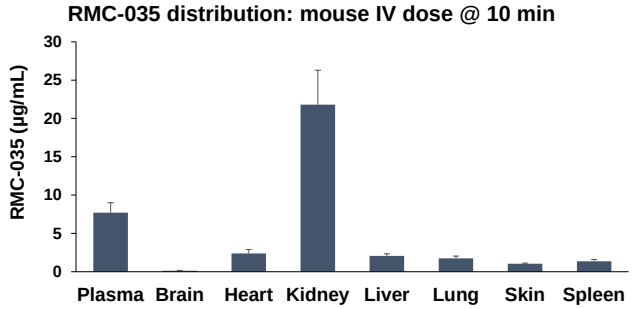
RMC-035 RAPIDLY DISTRIBUTES TO KIDNEYS & PRESENTS WITHIN PROXIMAL TUBULAR CELLS

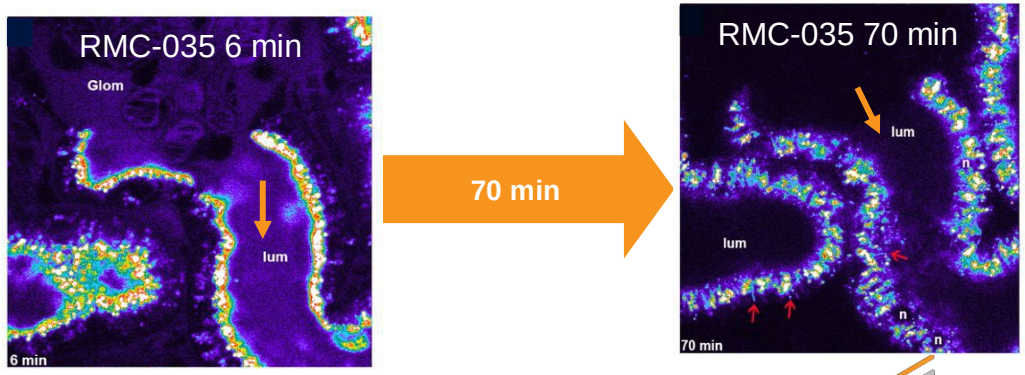
- RMC-035 preferentially distributes to target cells where AKI occurs
- Small proteins (like RMC-035) rapidly filtered by the kidney glomeruli
- Filtered RMC-035 is then reabsorbed by kidney tubules
- RMC-035 is present in tubule cells within an hour of administration

Radiolabeled RMC-035 preferentially distributes to the kidneys





Fluorescent-labelled RMC-035 internalized by kidney proximal tubular cells



Ahlstedt et al. (2015) Am J Nucl Med Mol Imaging. 5(4):333
Åkerström et al. (2019) Antiox Redox Signal. 30(4):489

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TOXICOLOGY EVALUATIONS OF RMC-035 SUPPORT AN ATTRACTIVE SAFETY PROFILE

- Safety profile evaluated in 4 GLP repeat dose toxicity studies
  - Rat, marmoset, cynomolgus monkey
- Findings were limited to mild kidney response
  - Expected from a small protein
  - Tubular deposition of drug at high doses – ‘protein overload’
- Toxicology program completed – data usage:
  - Support and adult development in CS-AKI & transplant to NDA/MAA
  - Indication, PK and short-term treatment nullifies data requirements for carcinogenesis/reproductive and/or developmental toxicology studies

NDA, new drug application; MAA, market authorization application; GLP, Good Laboratory Practice

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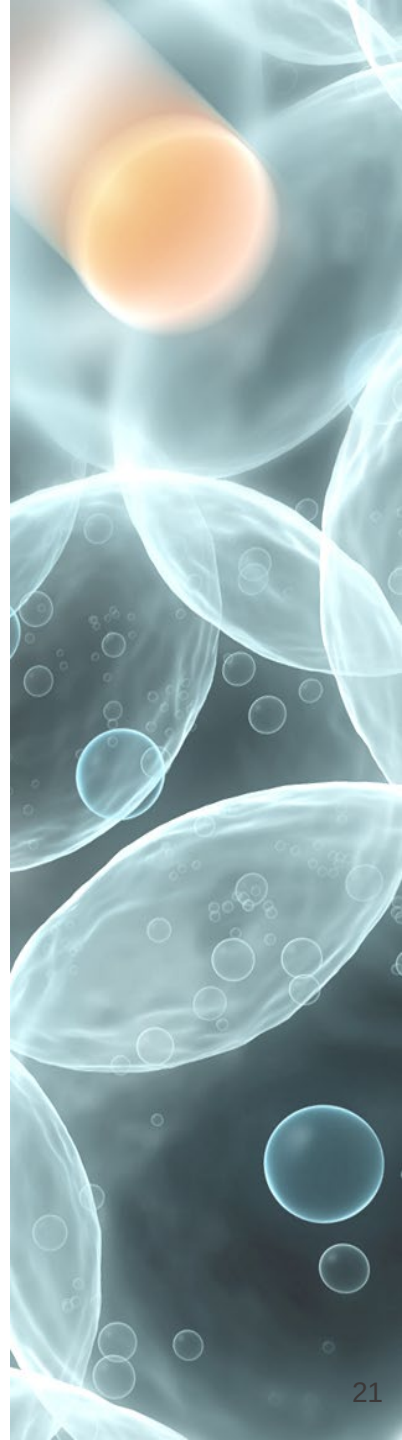
SUMMARY & CONCLUSIONS

- RMC-035 is a novel investigational drug in development for the prevention and early treatment of AKI
- Well characterized mode-of-action that targets key disease pathways in AKI
- Robust and reproducible efficacy in multiple disease models and species
  - Congruent in vitro and in vivo pharmacology
- Short half-life and rapid natural distribution to kidney tubular cells – the initial site of injury in AKI
- Modified naturally occurring protein with good safety profile
- Targets AKI upstream of cell injury – a unique treatment paradigm
- Indication choice (AKI) limits preclinical requirements up to NDA/MAA



GUARD THERAPEUTICS

Clinical experience with RMC-035

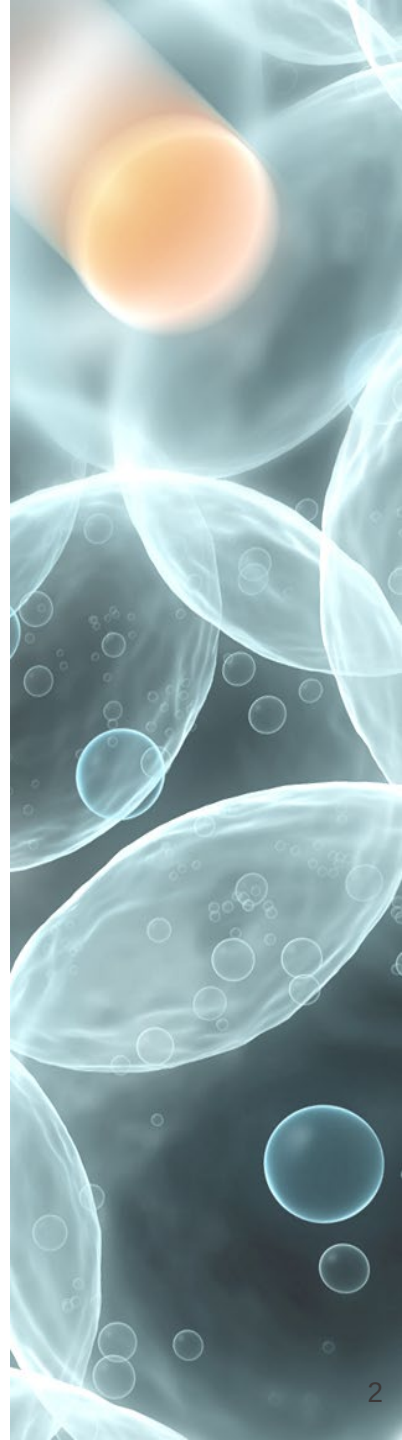
Capital Markets Day, Stockholm

September 21, 2022

Michael Reusch, CMO

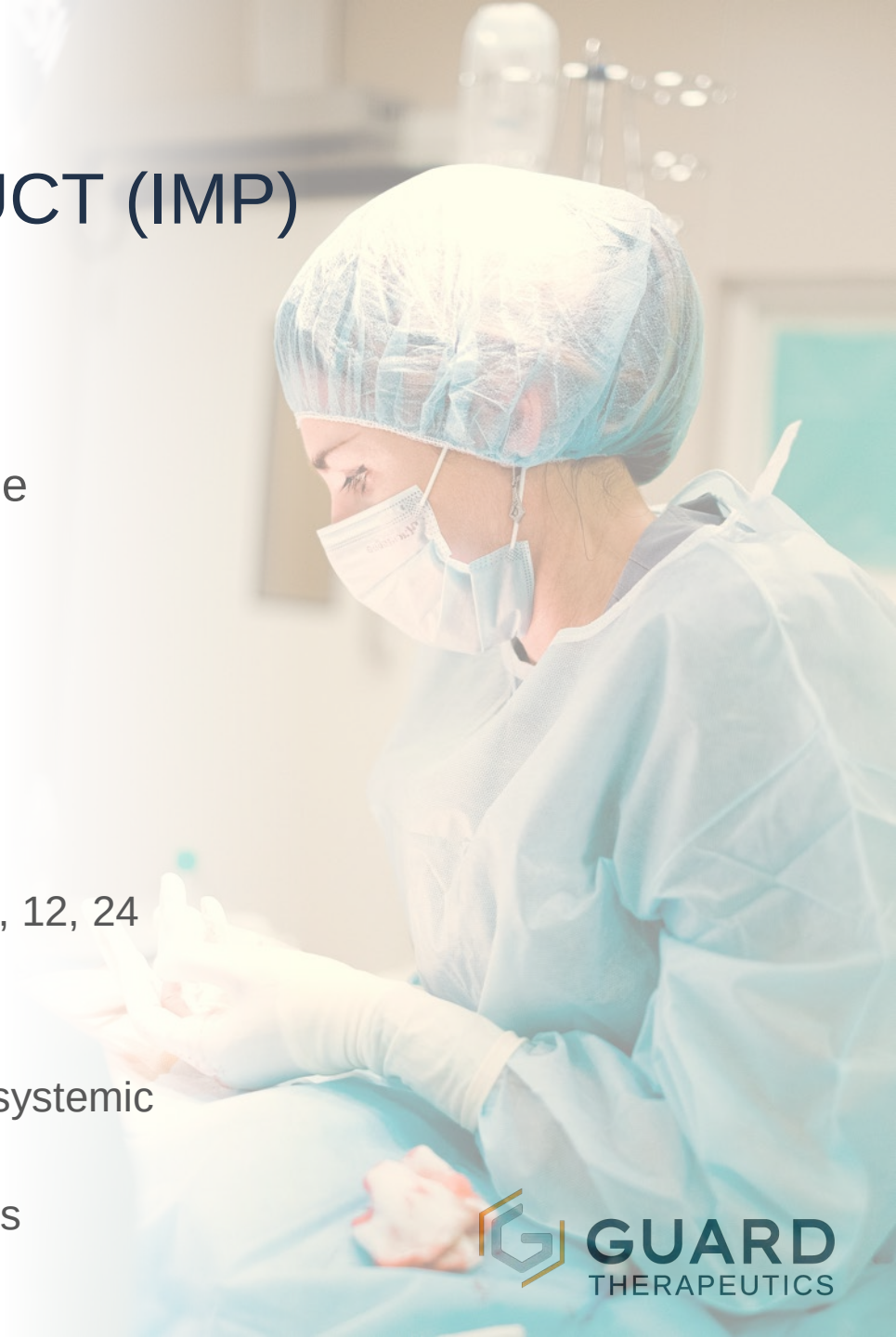
CLINICAL STUDIES OF RMC-035

Study	Phase	Population	Dosing	Key endpoints	Country	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
AKITA	Phase 2	Cardiac surgery	Multiple dosing (0.65 or 1.3 mg/kg)	Efficacy, safety	Europe, North America	Ongoing
ROS-06	Phase 1b	Kidney transplantation	Multiple dosing, variable dose (start dose 0.3 mg/kg)	Pharmacokinetics	Sweden	Ongoing



INVESTIGATIONAL MEDICINAL PRODUCT (IMP)

- Drug product is delivered to clinical sites as ‘Concentrate for solution for infusion’
- Diluted with NaCl solution to a set volume (50 mL) prior to use
- Intravenous (IV) administration at ICU/hospital
  - Central venous catheter (CVC)
  - Peripheral venous catheter (Phase 1 studies)
- Current dosing paradigm in cardiac surgery:
  - In total 5 doses (first dose during surgery, remaining doses at 6, 12, 24 & 48 hours after the first dose)
    - First infusion must start before cardio-pulmonary bypass
  - First 2 doses delivered as infusions over 60 minutes to extend systemic exposure
  - Remaining doses (3 to 5) delivered as infusions over 30 minutes



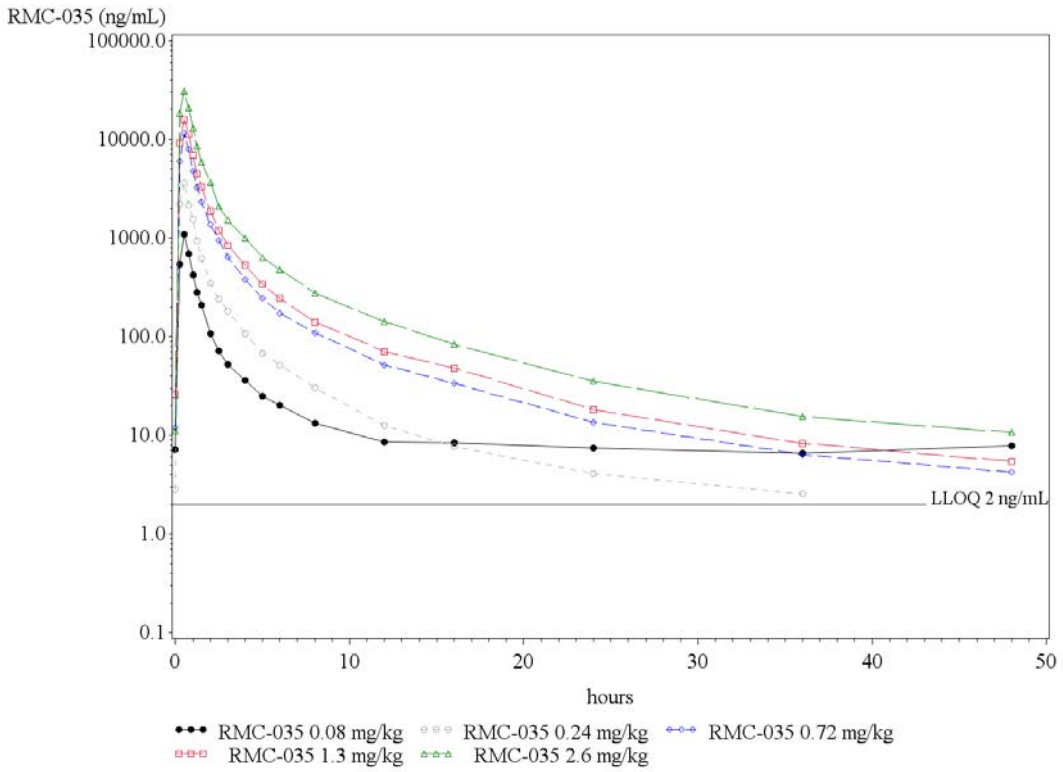
GUARD THERAPEUTICS

PHARMACOKINETICS (SAD STUDY) – RAPID INITIAL ELIMINATION PHASE AND DOSE PROPORTIONAL EXPOSURE

- T_{max} was 0.5 hours (end-of-infusion)
  - Observed in all dose groups
- Dose-proportional exposure for C_{max} and AUC_t across full dose range
- Multi-exponential plasma elimination phase
  - Rapid initial elimination
  - 70-80% decrease in plasma levels within 1 hour after end-of-infusion

RMC-035 plasma concentrations

Line plots geometric mean (all dose groups; full analysis set)



T_{max}: time of maximum plasma concentration: C_{max}: maximum plasma concentration; AUC_t: area under the curve total measured exposure; CV: coefficient of variation; $T_{½}$: plasma half-life; SAD: single ascending dose

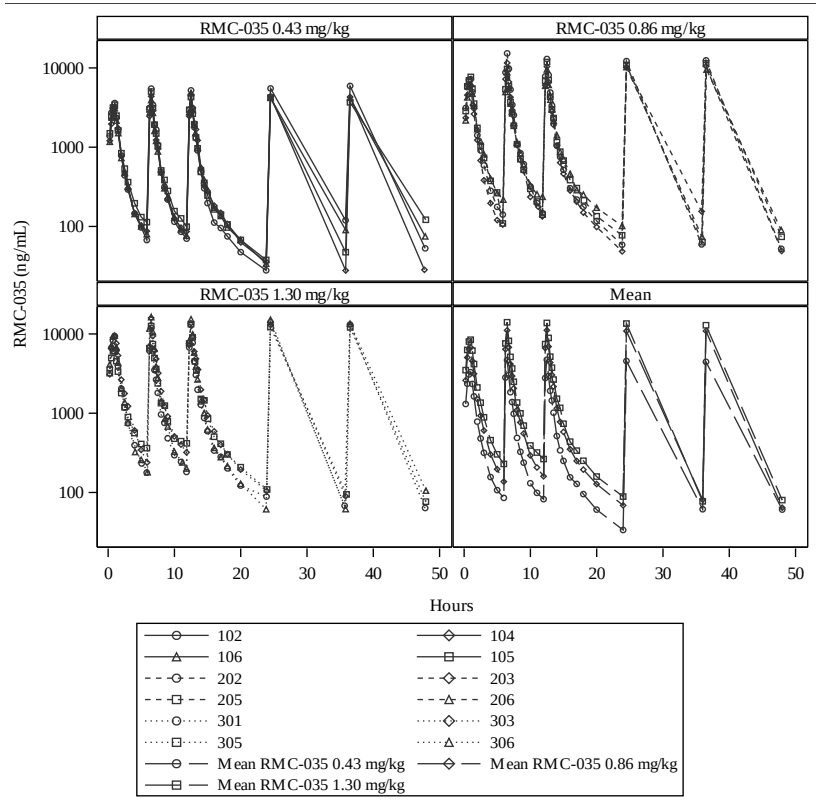
GUARD THERAPEUTICS

PHARMACOKINETICS (MAD STUDY) – DOSE LINEARITY AND NO DRUG ACCUMULATION

- T_{max} observed at end-of-infusion (30 or 60 min)
- C_{max} and $AUC_{0\text{-}24h}$ increased with dose
- Dose linearity across dose groups, with slightly lower exposures than predicted in highest (3rd) dose group
- No accumulation
  - ➢ Rapid initial elimination phase (as in SAD study)

RMC-035 Plasma concentrations

Logarithmic line plots 0-48h RMC-035 (ng/mL) (PK analysis set)

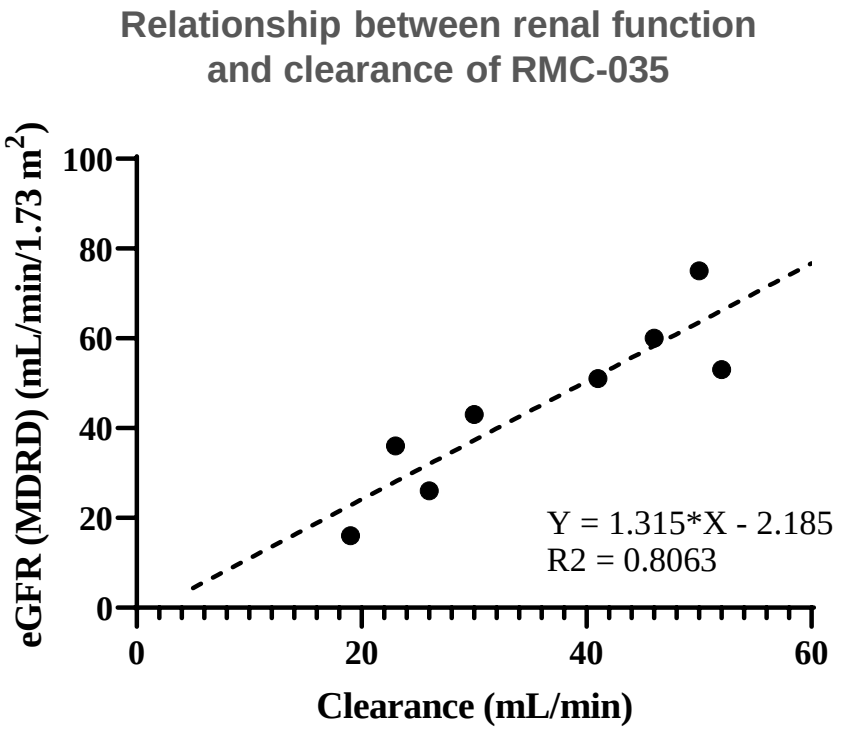


T_{max}: time of maximum plasma concentration: C_{max}: maximum plasma concentration; $AUC_{0\text{-}24}$: area under the curve 24h measured; CV: coefficient of variation; SAD: single ascending dose; MAD: multiple ascending dose; $T_{½}$: plasma half-life

GUARD THERAPEUTICS

RENAL IMPAIRMENT STUDY – RMC-035 EXPOSURE INCREASES WITH DECLINING RENAL FUNCTION

- Plasma clearance for RMC-035 (absolute & relative) generally decreased with declining renal function
- AUC ($AUC_{0\text{-last}}$ and $AUC_{0\text{-inf}}$) increased with declining renal function
  - AUC approximately doubles when renal function is reduced by 50%



Start dose in Phase 2 AKITA study dependent on renal function

$AUC_{0\text{-last}}$: area under the curve from dose to last measurement; AUC_{inf}: area under the curve extrapolated total exposure; eGFR: estimated glomerular filtration rate; MDRD: Modification of Diet in Renal Disease equation for eGFR

GUARD THERAPEUTICS

EARLY PHASE 1 STUDIES – FAVORABLE SAFETY AND TOLERABILITY PROFILE OF RMC-035

SAD study

- One serious adverse event (SAE) – not related to study drug
- Most frequently reported adverse events (AEs):
  - Nasopharyngitis: mostly mild – not related to study drug
  - Headache: 5 subjects on RMC, 1 on placebo; most events reported as possibly related to study drug

GUARD THERAPEUTICS

EARLY PHASE 1 STUDIES – FAVORABLE SAFETY AND TOLERABILITY PROFILE OF RMC-035

MAD study

- No SAEs

Most frequently reported AEs

- Local infusion site reactions (majority of subjects treated with RMC-035)
- Headache (5 on RMC-035, 3 on placebo)
- Nausea (5 subjects on RMC-035; most events reported as possibly related to study drug)

Renal impairment study

- Only one AE in the study of mild severity (feeling cold)

No safety signals of concern in Phase 1 studies of RMC-035

GUARD THERAPEUTICS

ROS-04 – FIRST STUDY IN CARDIAC SURGERY PATIENTS

- Small Phase 1b pharmacokinetics and safety study in target patient population – de-risks Phase 2 (AKITA) study
- Exploratory analysis of urine biomarkers – renal tubular cell stress/injury markers
  - Note: study not powered for this analysis

OVERVIEW OF STUDY ROS-04	
DESIGN	Randomized, double-blind
OBJECTIVES	Primary: safety; Secondary: pharmacokinetics (PK); Exploratory: biomarkers
PRIMARY ENDPOINT	Safety profile (adverse event reporting)
STUDY SUBJECTS	Subjects undergoing non-emergent open-chest cardiac surgery at high risk to develop CS-AKI
CONTROLS	Placebo
SAMPLE SIZE	12 (8 on RMC-035 & 4 on placebo)
DURATION	Recruitment period: Q1-2 2021

GUARD THERAPEUTICS

ROS-04: OVERVIEW SAFETY REPORTING

- 23 AEs in total (following reconciliation of reported and measured events)
  - Majority of AEs were mild or moderate in severity
  - 18 AEs were treatment-emergent (i.e., occurring within 3 days after last dose)
- 7 SAEs reported in 4 subjects
  - RMC-035: 5 SAEs in 3 subjects
  - Placebo: 2 SAEs in 1 subject
  - 5 SAEs were treatment-emergent
    - Pericardial tamponade (n=1), AKI (n=2), pericardial effusion (n=1), pneumonia (n=1)
- No AEs were related to study drug or led to withdrawal of study drug

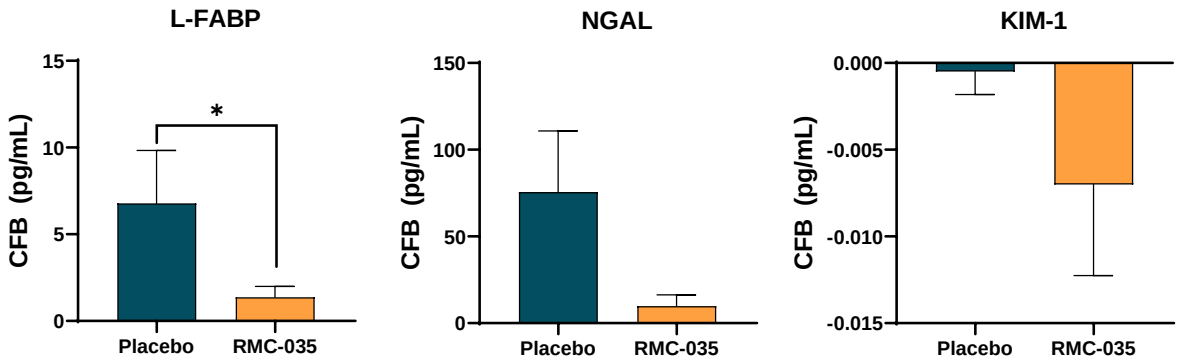
Frequency and type of events as expected following cardiac surgery

GUARD THERAPEUTICS

BIOMARKER RESPONSE INDICATE REDUCED KIDNEY CELL INJURY WITH RMC-035 TREATMENT

- Panel of urine biomarkers reflecting renal tubular cell stress and/or injury
  - Measured pre-dose & 4 hours after onset of surgery to capture intra-operative stress
- Renal cell injury biomarkers:
  - Liver fatty acid binding protein (L-FABP)
  - Neutrophil gelatinase associated lipocalin (NGAL)
  - Kidney injury molecule-1 (KIM-1)

Urine markers of cell injury – change from baseline at 4 hours



CFB = change from baseline

* p<0.05
n=4 (Placebo)
n=8 (RMC-035)

Expected early rise of kidney cell injury markers L-FABP & NGAL was blunted with RMC-035 treatment

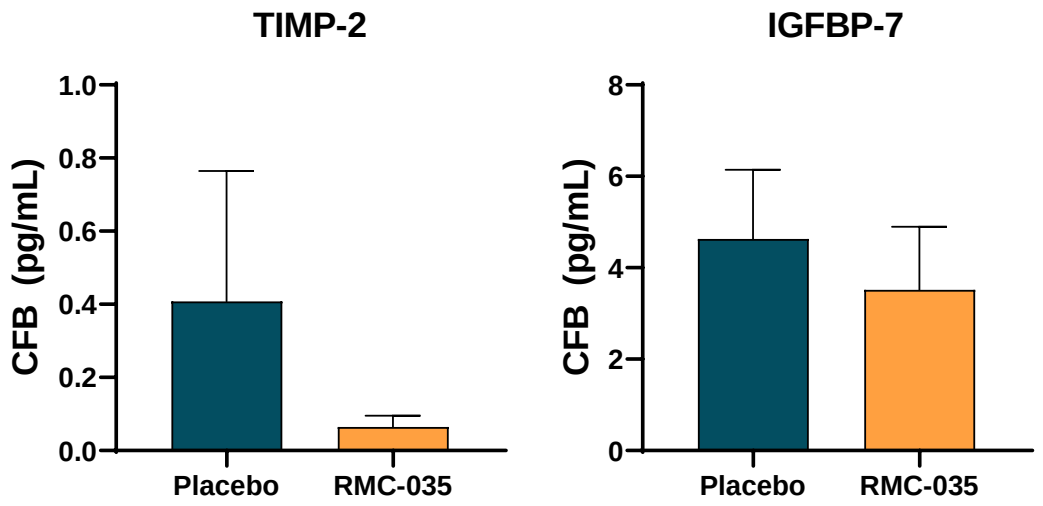
GUARD THERAPEUTICS

Study report 20-ROS-04-UBM

BIOMARKER RESPONSE INDICATE REDUCED KIDNEY CELL STRESS WITH RMC-035 TREATMENT

- Renal cell stress markers: tissue inhibitor of metalloproteinase -2 (TIMP-2) and insulin growth factor binding protein (IGFBP-7)
  - ➢ These markers are FDA-approved to predict onset of AKI (NephroCheck®)
- 4-hour timepoint most relevant to determine perioperative cell stress/injury

Urine markers of cell stress – change from baseline at 4 hours



n=4 (Placebo)
n=8 (RMC-035)

All biomarkers of kidney cell injury/stress demonstrated a numerical reduction as compared to placebo, in alignment with RMC-035 mechanism

Study report 20-ROS-04-UBM

GUARD THERAPEUTICS

SUMMARY & CONCLUSIONS OF PHASE 1 PROGRAM

- RMC-035 has well-targeted mechanisms with preferential biodistribution to the kidney
  - Ideal for AKI prevention and treatment
- In total 52 subjects exposed to RMC-035 in four studies (ROS-01 to -04)
  - Healthy subjects (n=36)
  - Renally impaired subjects (n=8)
  - Cardiac surgery patients (n=8)
- Predictable and consistent PK profile with rapid initial elimination from plasma (due to glomerular filtration)
  - Dose linearity, no accumulation
  - Total exposure (AUC) increases with declining renal function
- RMC-035 assessed as safe and generally well tolerated across study populations
- Biomarker signal supports reduced peri-operative kidney cell injury

GUARD THERAPEUTICS

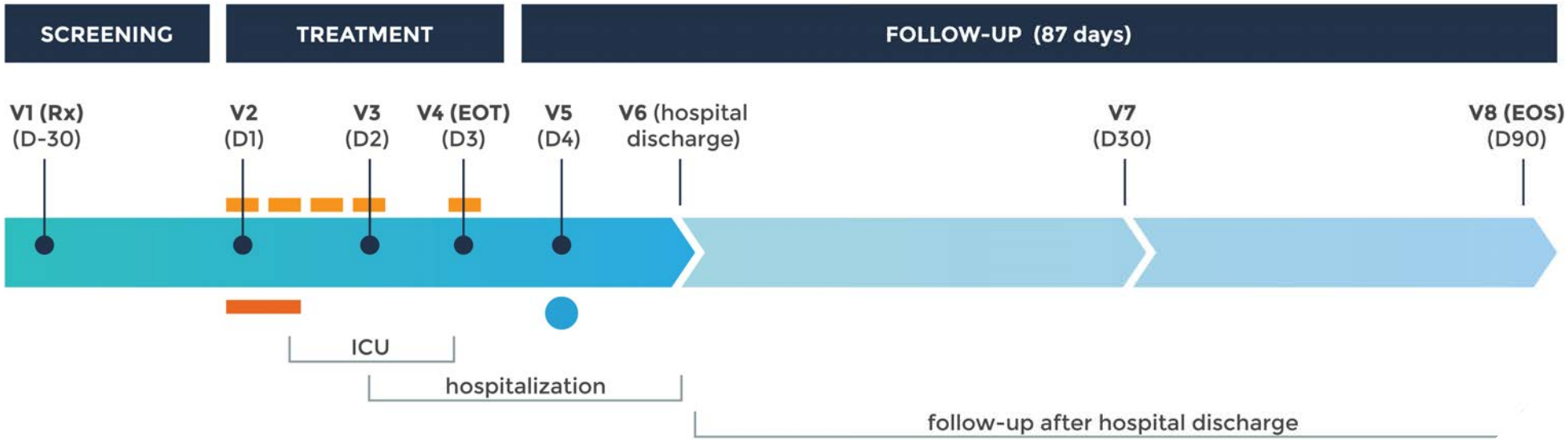
GLOBAL PHASE 2 STUDY (AKITA) – DESIGN

- Objective is to evaluate the efficacy & safety of RMC-035 in subjects at high risk of developing AKI following open-chest cardiac surgery
- Randomized, placebo-controlled, double-blind, adaptive, parallel group
- 268 subjects in total (1:1 randomization RMC-035:placebo)
- Two starting doses dependent upon kidney function
- Primary endpoint is AKI as per Kidney Disease Improving Global Outcomes (KDIGO) guidelines within 72 hours after surgery
- Key secondary (efficacy) endpoints include:
  - Post-baseline changes in renal function
  - Severity/duration/persistence of AKI
  - Dialysis treatment; length of hospital & ICU stay
  - MAKE (major adverse kidney events: either death, dialysis or ≥25% eGFR decline)

Study design will facilitate informed decision about optimal Phase 3 design

KDIGO clinical guidelines issued by International Society of Nephrology

AKITA STUDY – OVERVIEW



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

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

AKITA study has operational advantages as compared to chronic indications, including alignment with standard-of-care, short treatment period and limited follow-up period

STUDY POPULATION – CARDIAC SURGERY AT RISK FOR AKI

- Adult patients up to age 84 years
- Scheduled for non-emergent surgery with use of cardiopulmonary bypass:
  - Coronary Artery Bypass Graft (CABG) surgery
  - AND/OR valve surgery (single or multiple valves)
  - AND/OR ascending aorta aneurysm surgery
  - AND AKI risk factors† present
    - One type of surgery: at least two AKI risk factors OR eGFR<60 mL/min/1.73m^2 alone
    - Combined surgery: at least one AKI risk factor

† **AKI Risk factors include:**
- Left ventricular ejection fraction (LVEF) <35%
- Repeat surgery/history of open chest cavity cardiac surgery
- Type 2 diabetes mellitus
- Age ≥70 years
- Heart failure
- History of AKI
- Anemia with hemoglobin ≤11 g/dL
- Albuminuria
- Estimated glomerular filtration rate is <60 mL/min/1.73 m^2

AKITA

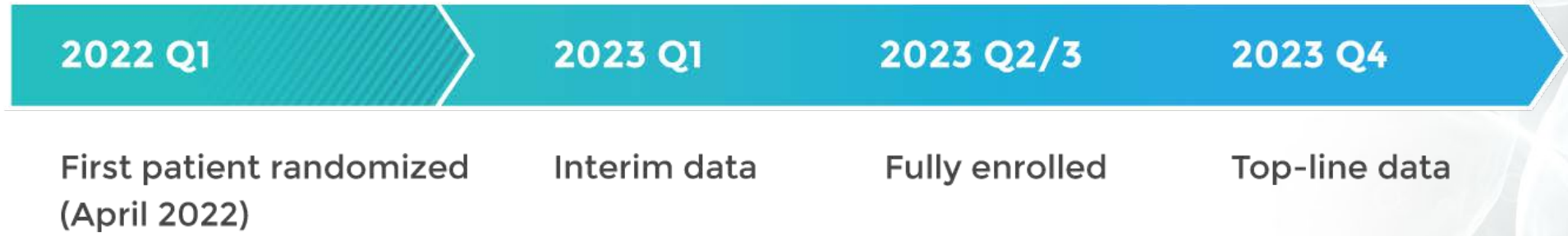
GUARD THERAPEUTICS

BLINDED INTERIM ANALYSIS WILL BE PERFORMED AFTER 134 PATIENTS – OUTCOME EXPECTED IN Q1 2023

- Independent Data Monitoring Committee (DMC) will perform blinded interim analysis when 134 subjects have completed study visit at 72 hours after surgery
- Conditional power (CP) calculated based on primary endpoint
- Key secondary endpoints considered if prespecified criteria are not met for study continuation
- Principal outcomes of analysis:
  - Study continuation as planned (i.e., n=268)
  - Sample size expansion to maximum 348 subjects
  - Termination for safety/futility (no formal pre-specified criteria)

AKITA STUDY IS PROGRESSING ON TRACK

- Currently 53 patients randomized
- Recruitment in line with projections
- Sites open in Canada, Czech Republic, Germany, Spain



FRAMEWORK OF PIVOTAL PHASE 3 TRIAL

- One pivotal Phase 3 study is sufficient for registration
- FDA tentatively agreed to conduct an adaptive and seamless Phase 2b/3 study
  - Phase 2b = find optimal therapeutic dose
  - Phase 3 = confirm therapeutic effect
- Dose-finding based on acute endpoint (e.g., within 7 days after surgery)
- Similar design as AKITA study – powered for MAKE endpoint
  - No need for assessment of long-term safety
- Conservative estimate of sample size is 150–200 (P2b) + 600–800 (P3)
  - Data-driven evaluation following AKITA results on optimal P2b/3 design
  - Opportunity for optimizing patient population (e.g., targeting CKD patients)

AKITA study provides opportunity to set optimal Phase 2b/3 design

GUARD THERAPEUTICS

MAKE: Major Adverse Kidney Events

OVERALL SUMMARY AND CONCLUSIONS

- RMC-035 has targeted mechanisms and biodistribution profile ideal for the treatment of CS-AKI
- Comprehensive Phase 1 program of four separate studies
  - No safety signals of concern
  - Provides data to support indication expansion to other AKI patient groups
  - Biomarker results supporting pharmacodynamic effect of RMC-035 with protection of kidney (tubular) cells
- Ongoing recruitment in large global Phase 2 AKITA study with expected interim analysis in Q1 2023 & full results in Q4 2023
- AKITA study provides the basis for
  - Initiation of one pivotal (P2b/3) study in CS-AKI
  - Optimized and data-driven design of P2b/3 study

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Clinical strategy for RMC-035 in kidney transplantation

Capital Markets Day, Stockholm

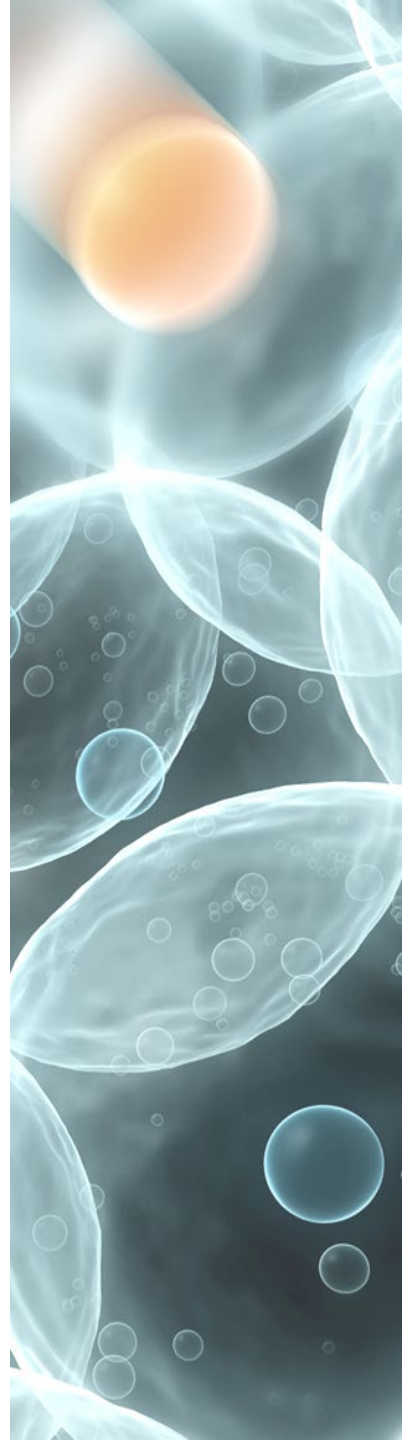
September 21, 2022

Michael Reusch, CMO

OPPORTUNITY FOR RMC-035 IN KIDNEY TRANSPLANTATION

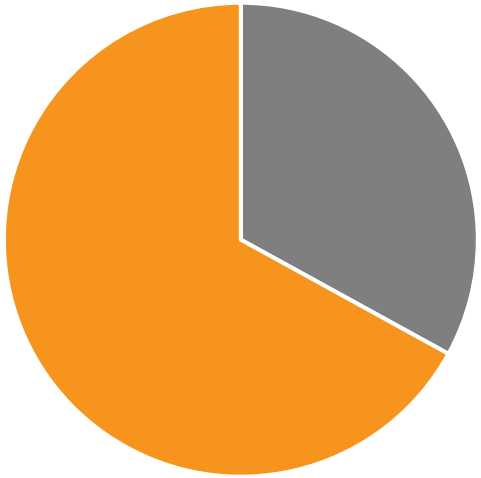
- Large unmet medical need to protect kidney graft and improve long-term clinical outcomes (including graft function)
- Significant commercial opportunity in relation to anticipated size of development program
  - Initial addressable patient population in US & EU ~20,000 patients
    - ~40,000 deceased donor kidney transplantations
    - ~ 50% assessed as “high risk” and target for treatment
  - Total market opportunity in US & EU5 assessed as >$300M
- No approved drugs and limited competition
- Solid scientific rationale, preclinical proof-of-concept established
- Clear regulatory pathway
  - Endpoint acceptability
  - Orphan Drug Designation opportunity

Palmisano et al. J Clin Med (2021)

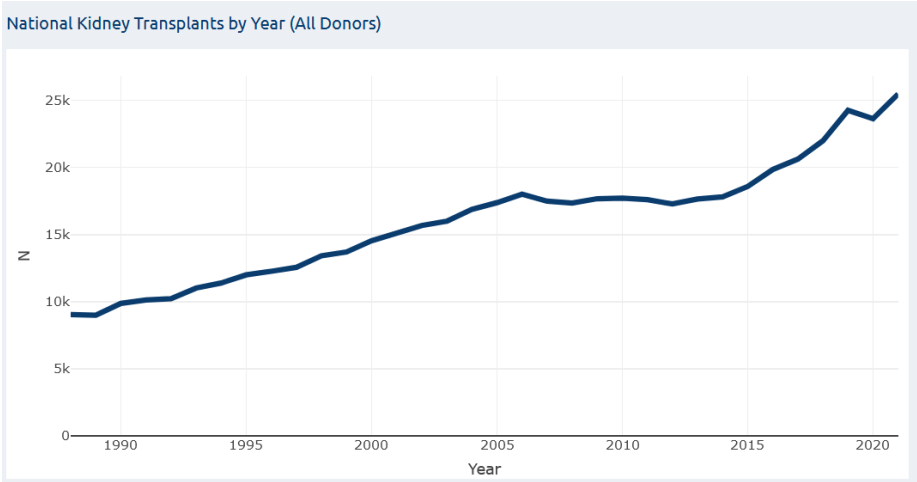


OVER 40,000 DECEASED DONOR KIDNEY TRANSPLANTATIONS ARE PERFORMED ANNUALLY IN US/EU

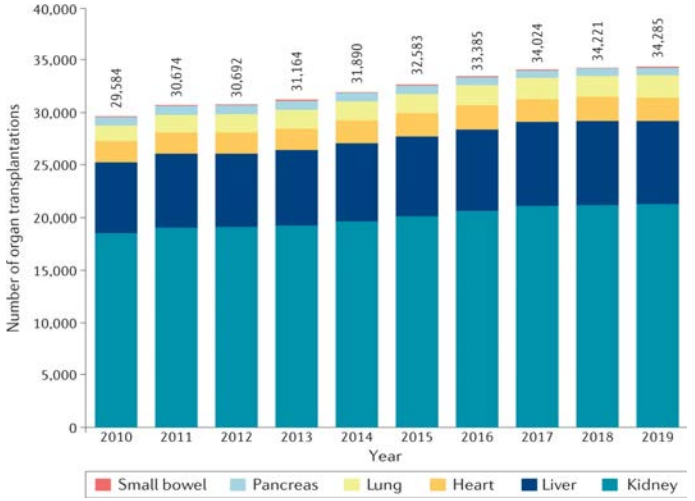
Kidney transplantations performed with deceased donor (cardiac death, brain death)



US: National Kidney Transplants by Year (All Donors)



EU: Number of organ transplantations performed between 2010 and 2019



https://insights.unos.org/OPTN-metrics/; Vanholder et al. Nature Reviews Nephrology **volume 17** (2021)

GUARD THERAPEUTICS

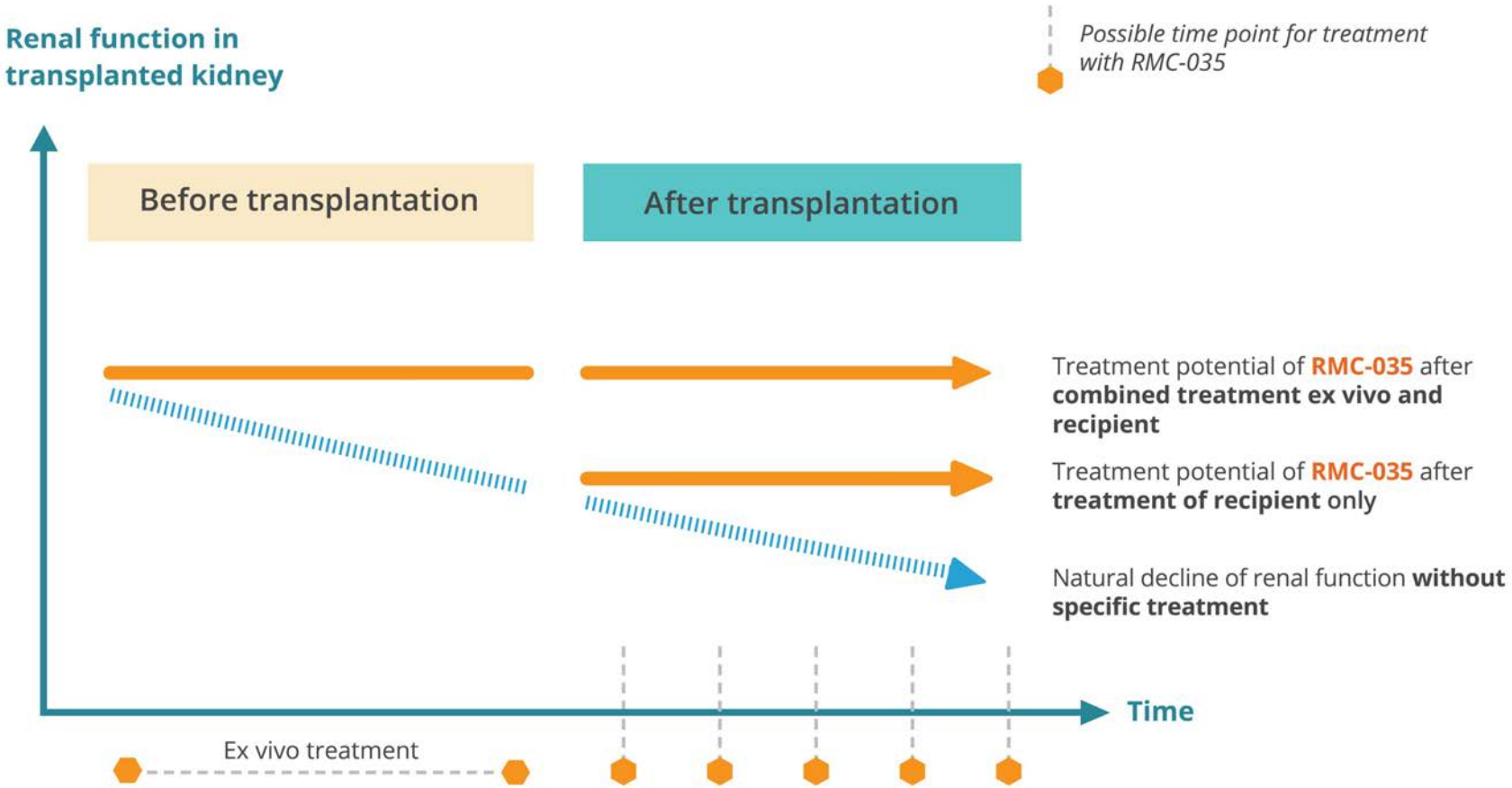
MEDICAL NEED & SCIENTIFIC RATIONALE FOR RMC-035 IN KIDNEY TRANSPLANTATION

- High rate of extensive ischemic injuries in kidney grafts
  - Similar to cardiac surgery
  - Ischemia/IRI* arises during organ procurement, ex vivo storage and graft re-perfusion in transplant recipients
- Clinical manifestations of AKI = delayed graft function (DGF)
  - Dialysis requirement, prolonged hospital stay, complex post-operative management
- Target is prevention of long-term DGF complications
  - Decreased graft function
  - Shorter graft survival
  - Increased mortality
- Synergies
  - Overlapping pathophysiology between renal graft injury and CS-AKI
  - RMC-035 mechanism-of-action and available nonclinical data supportive
  - Data from healthy subjects and renally impaired subjects already available

Palmisano et al. J Clin Med (2021); Mannon Nephron (2019); *IRI; Ischemica-Reperfusion-Injury

GUARD THERAPEUTICS

RMC-035 TREATMENT – OPPORTUNITY TO REDUCE KIDNEY GRAFT INJURIES EX VIVO & IN RECIPIENT



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CLEAR REGULATORY PATH WITH ORPHAN OPPORTUNITY

- FDA views prevention of DGF as a priority indication
  - FDA Guidance for Industry 2019
- Orphan Drug Designation opportunity
- No approved drugs for prevention of DGF/improvement of kidney graft function
  - Placebo comparison accepted
- Acceptable endpoints for registration
  - Reduction of DGF (traditionally defined as dialysis requirement within 7 days following transplantation)
  - More recently FDA accepts kidney graft function (eGFR) assessed at 1 year after transplantation
- Synergy with CS-AKI program

GUARD THERAPEUTICS

HIGH LEVEL CLINICAL DEVELOPMENT PLAN

Small
P1b study

Small PK study to establish exposure in transplanted patients

- Single-site
- 8-12 patients
- Open-label, non-comparative
- Clinical trial approval obtained in Sweden

Currently enrolling patients

Exploratory
P2 study

Generate efficacy data and establish proof-of-concept for a 3-month endpoint

- Around 60 patients (1:1 randomization active vs placebo)
- Faster evidence of effect compared to full proof-of-concept study
- De-risks Phase 3 trial

Pivotal
P3 study

Proceed to pivotal study with efficacy signal on eGFR

- Adaptive P2b/3 approach
- Interim analysis with futility component
- One pivotal study
- Anticipated size 300-600 patients

GUARD THERAPEUTICS

FIRST TRANSPLANT STUDY (ROS-06) ONGOING – MAIN OBJECTIVES

Study	Phase	Population	Dosing	Key endpoint	Country	Status
ROS-06	Phase 1b	Kidney transplantation	Multiple dosing, variable dose (start dose 0.3 mg/kg)	Pharmacokinetics	Sweden	Ongoing

Study objectives

Primary

- Key pharmacokinetic parameters
  - Total exposure (AUC) most relevant

Secondary

- Additional PK parameters
- Safety

Exploratory

- Renal function
- Immunogenicity

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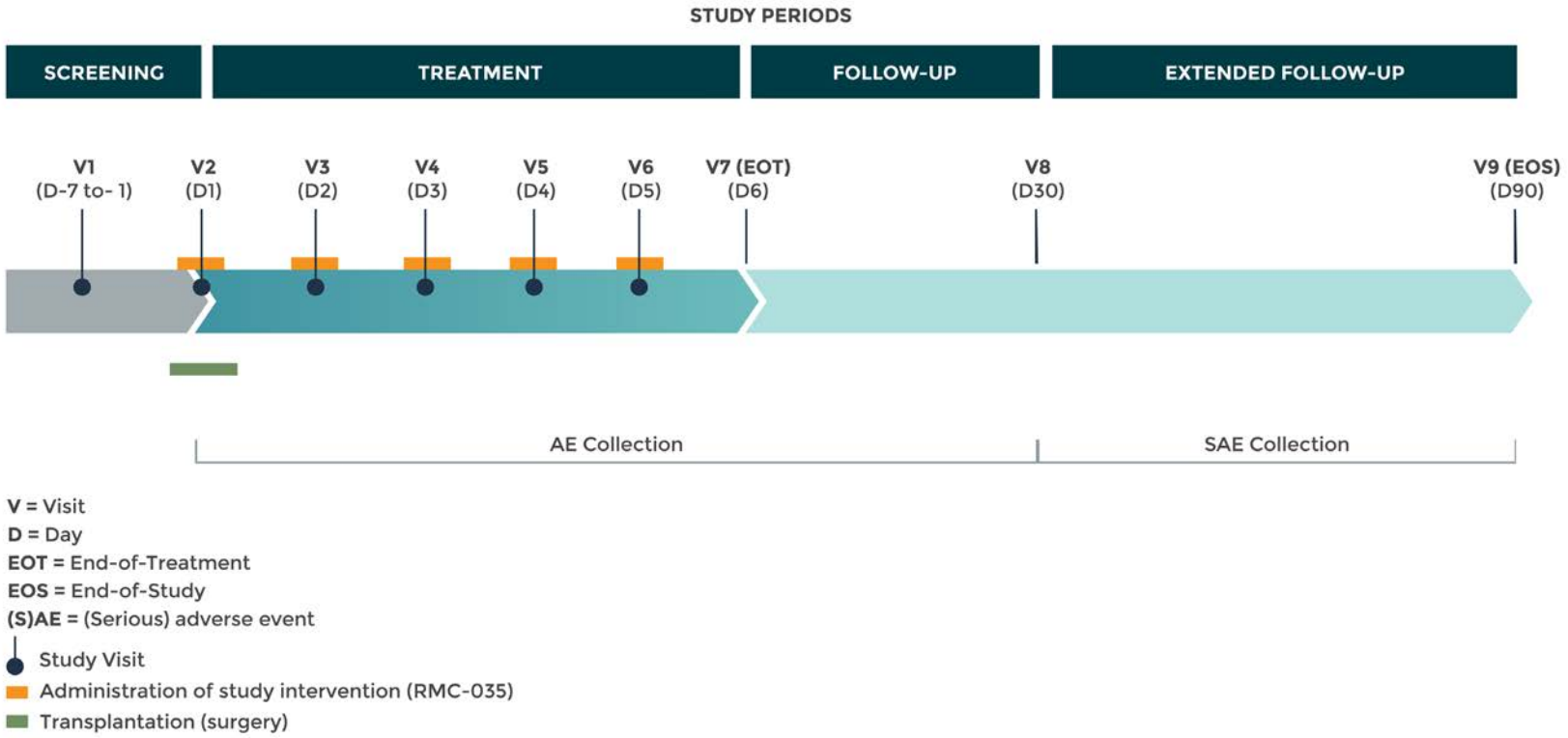
PHASE 1B STUDY (ROS-06) – DESIGN OVERVIEW



	Dose group 1 (4 patients)	Dose group 2 (4 patients)	Optional Dose group 3
Dose 1-2	0.3 mg/kg	0.3 mg/kg	To be determined
Dose 3-5	0.3 mg/kg	0.6 mg/kg	To be determined

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STATUS PHASE 1B STUDY (ROS-06)

- Single site study in Stockholm, Sweden
  - Executed in close collaboration with transplant surgeons at the Karolinska Institutet
- First patient enrolled in September 2022
- Interim analysis of the PK properties of RMC-035 following enrolment of two dose groups (8 patients)
  - Decision on need for an additional third dose group
- Full study results expected H1 2023
- Development of Phase 2 study protocol ongoing
  - Submission of clinical trial application for Phase 2 study based on interim results may be possible

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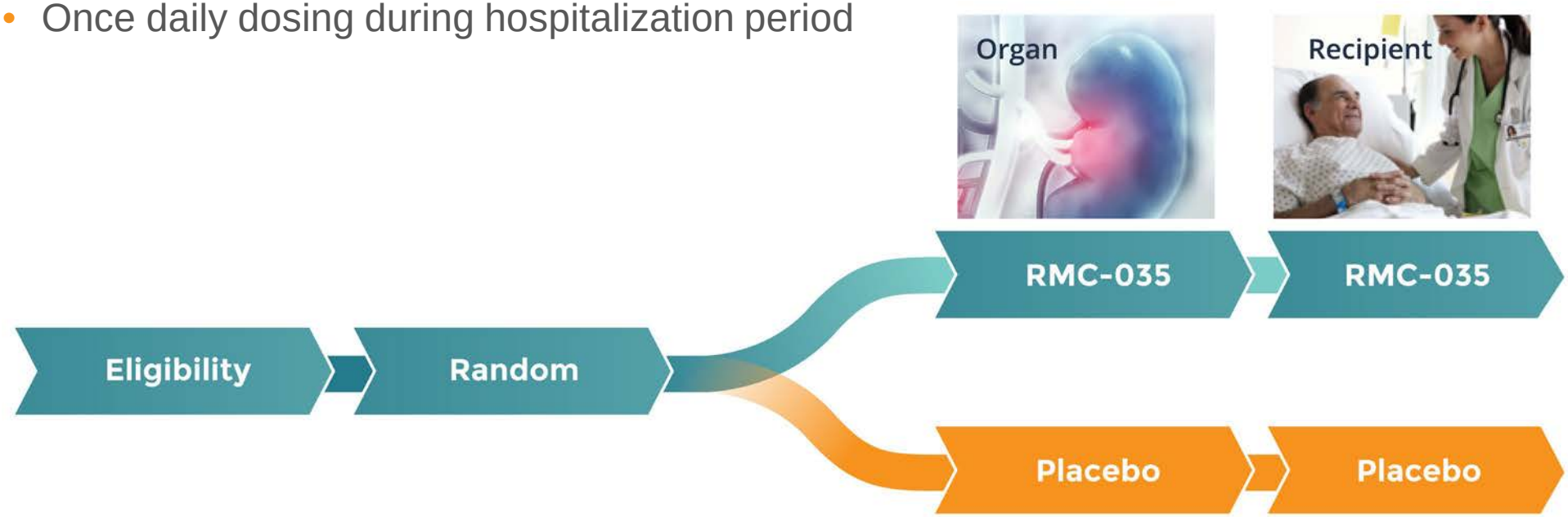
PHASE 2 STUDY TARGETS A DUAL TREATMENT CONCEPT

- Ex vivo treatment of kidney graft (via back-table perfusion or static cold storage solution)
- Recipient treatment
- First recipient dose during surgery
- Once daily dosing during hospitalization period



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BLUEPRINT FOR PHASE 2 STUDY

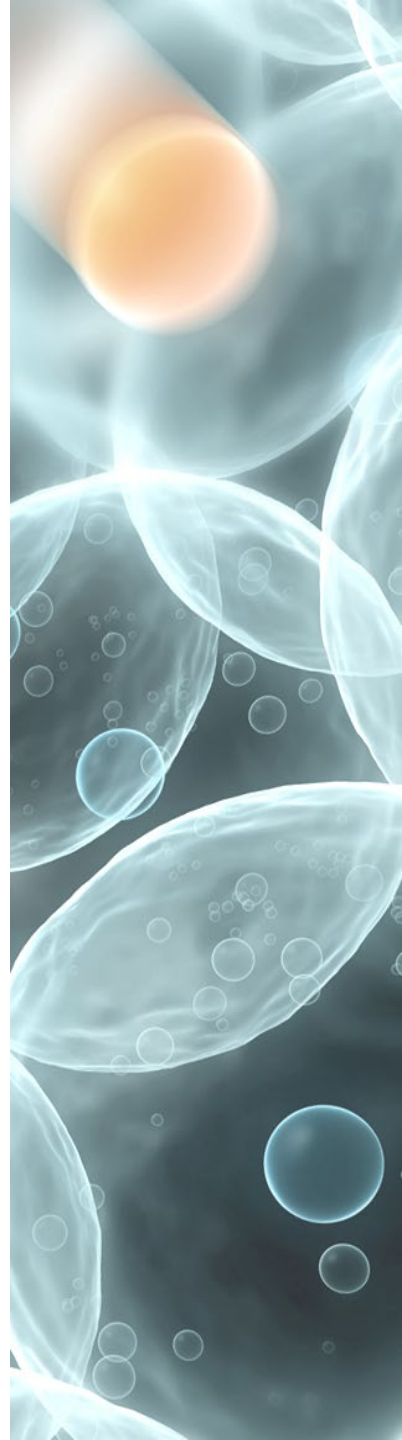
- Design discussions with global experts in US/EU (ongoing)
- Multi-center study – European centers only
- Randomized, placebo-controlled, double-blind, parallel group
- One active dose arm and placebo
- Key eligibility criteria
  - Recipient of a transplant from a deceased donor (brain death or cardiac death criteria)
  - Kidney graft is to be preserved by static cold storage
  - Criteria for DGF risk required (enrichment for high DGF risk)
- Primary endpoint is kidney function (eGFR at 3 months after transplantation)
  - Potential for long-term follow-up
- Renal imaging, biopsies, urine biomarkers considered as secondary endpoints

GUARD THERAPEUTICS

SUMMARY AND CONCLUSION

- Prevention of DGF and protection of kidney graft function is a large unmet medical need
  - Short-term and long-term complications (e.g., dialysis need, mortality)
- Attractive development with clear regulatory pathway to approval
- Large commercial opportunity in relation to anticipated size of development program
- No approved drugs and limited competition
  - No clinical development programs in late stage targeting DGF/renal function
- Strong scientific rationale & available data with RMC-035
  - Overlapping disease pathways in CS-AKI and DGF in kidney transplantation

Available clinical data of RMC-035 enables rapid progression to Phase 2



GUARD THERAPEUTICS

Market considerations – pricing & reimbursement

Capital Markets Day, Stockholm

September 21, 2022

Tobias Agervald, CEO

US MARKET & PRICING OPPORTUNITIES – IN SHORT

- Burden of CS-AKI after cardiac operations is well documented – cost exceeds ~$1B annually in the US only
- In-patient hospital reimbursement expected via a bundled payment system termed diagnosis related group (DRG) or case rate
  - CABG is one of the top DRG margins for US hospitals
- RMC-035 has potential for New Technology Add-on Payment (NTAP)
- Anticipated product price at ~$5k to $7.5k per treatment according to US Hospital Pharmacy & Treatment (P&T) members
- ~$15k to $20k per treatment attainable for hospital formulary inclusion in more circumscribed patient population (e.g. chronic kidney disease -CKD)
- Market opportunity in the US only is projected to **~$500M-$750M**

Global market opportunity well above $1B adding EU, JP & ROW

GUARD THERAPEUTICS

CS-AKI IS A SIGNIFICANT FINANCIAL BURDEN FOR HOSPITALS WITH ANNUAL COST IN THE US ~$1B

~$1B
in annual incremental hospitalization cost for CS-AKI patients

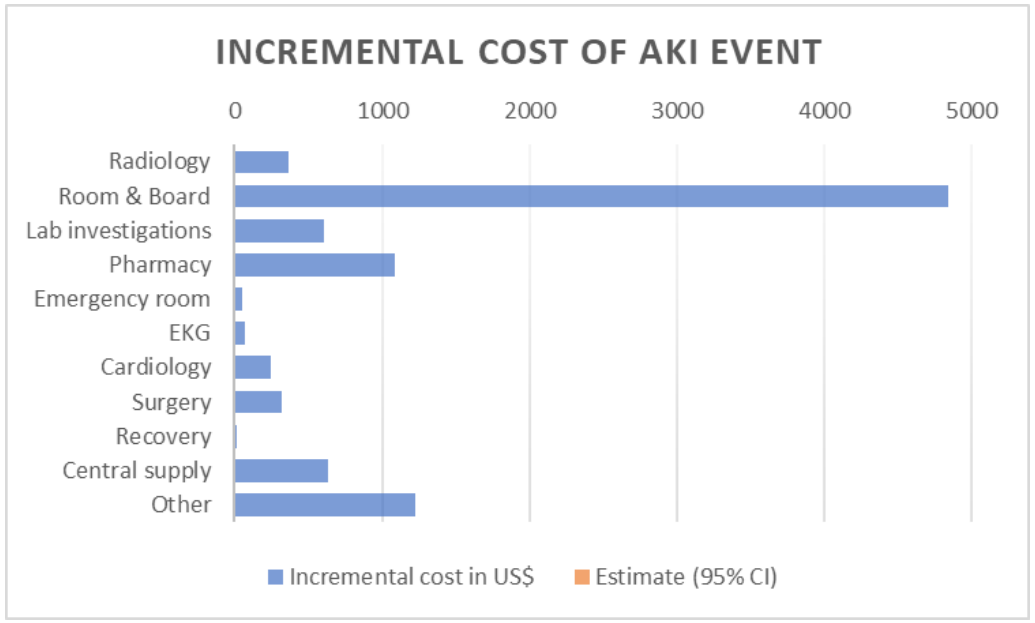
~$40k
in additional costs per hospitalization for CS-AKI

~6 day
average increase in length of stay for AKI patients

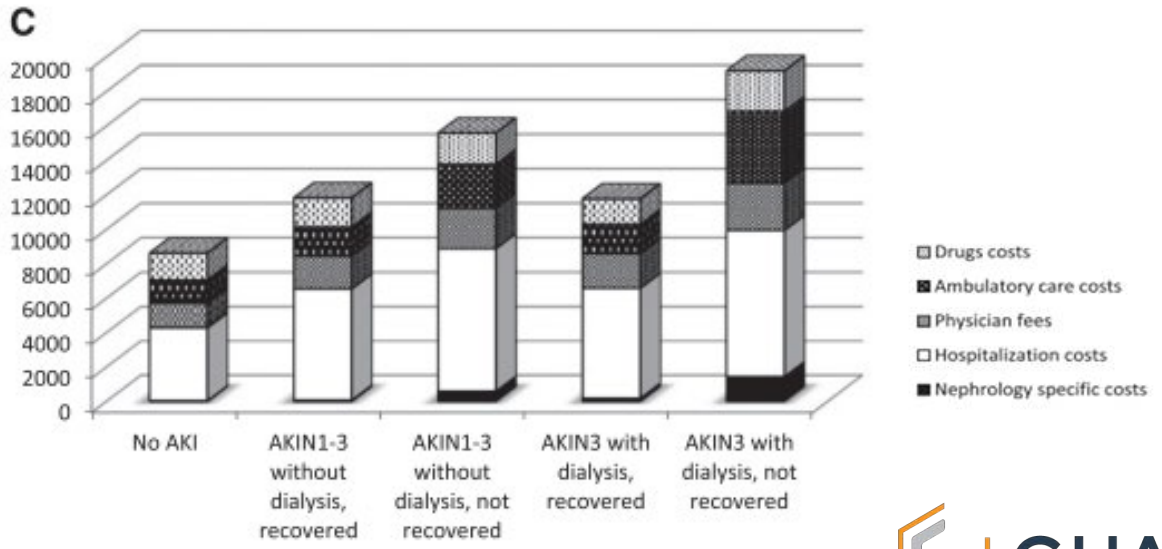
~$5,000
Average cost for a day in ICU

~$2,500
Average cost for a day in the hospital

The incremental cost of an AKI event following cardiac procedures in the US is largely driven by length of stay



Costs for nephrology care in the 90-days to 1-year following hospital admission is significantly higher for patients with AKI (Canadian dollars)



Sources: External analysis (Draft report, September 2022) & prior work, expert interviews; https://www.nephrocheck.com/global/aki-detection-urgency/, Ann Thorac Surg. 2018 Feb;105(2):469-475, Am J Cardiol. 2020 Jan 1;125(1):29-33, Clin J Am Soc Nephrol. 2017 Nov 7;12(11):1733-1743

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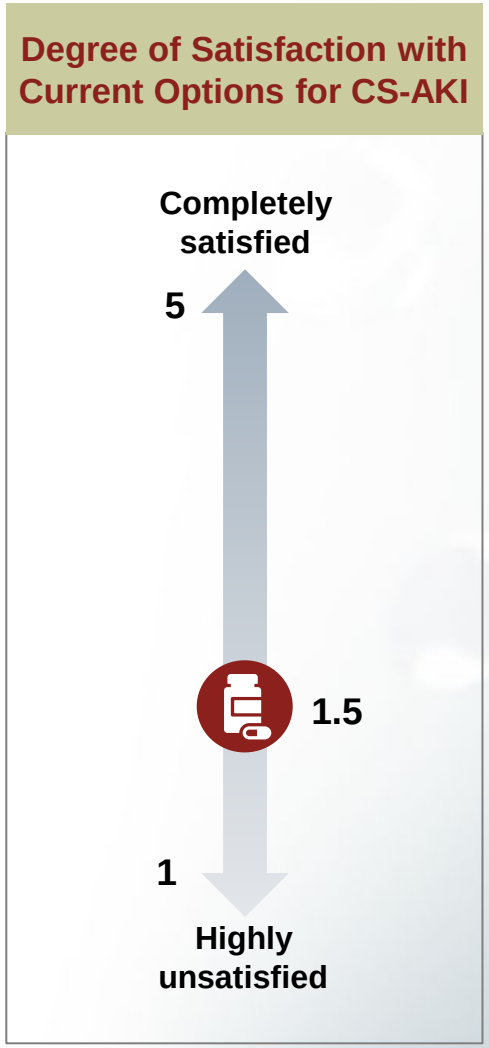
LARGE DISSATISFACTION WITH CURRENT LACK OF THERAPIES IN CS-AKI

- No available treatment options
- No relevant off-label therapies

> *"**Current options for CS-AKI are very poor**" – US Interventional Nephrologist*

> *"I am **highly unsatisfied with current options for CS-AKI**… the situation is even worse for CKD patients, who account for ~15-20% of our patients if you use a liberal definition"– US Cardiothoracic Surgeon*



CKD = Chronic Kidney Disease

Sources: External analysis (Draft report, September 2022), expert interviews

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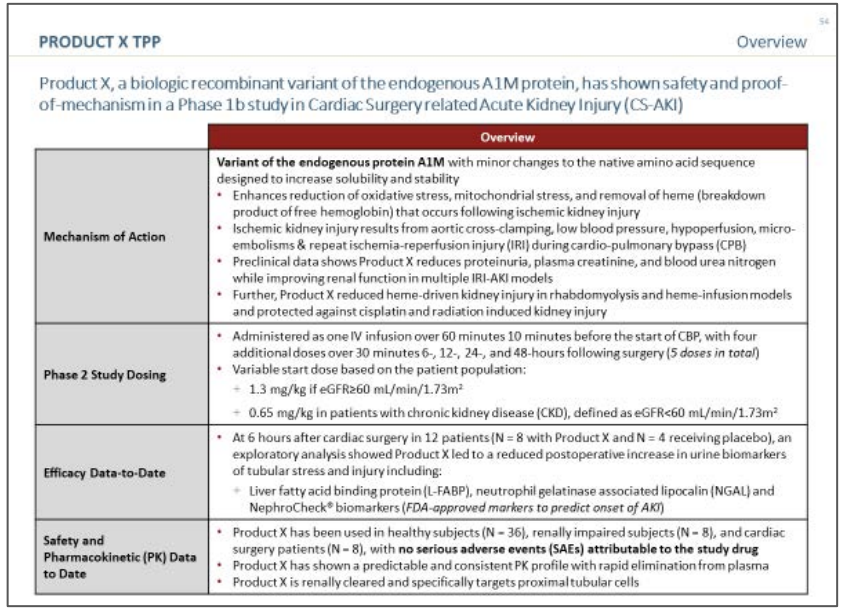
RMC-035 MECHANISM & TARGET PRODUCT PROFILE VIEWED FAVORABLY BY CLINICIANS

- Target product profile (TPP) of RMC-035 viewed favorably by clinicians: large unmet medical need & financial burden of AKI
- RMC-035 mechanism viewed as novel & clearly differentiated – not a “me-too drug”
- Highlighted importance of endpoints such as length of hospital stay, length of ICU stay, dialysis requirement
  - CS-AKI is a key performance indicator at most US hospitals
- Strong interest in subgroup of patients with CKD
  - Medicare spending for CKD patients >65 years old exceeded $50B in 2014, with a significant portion of spending allocated to dialysis patients



PRODUCT X TPP — Overview

Product X, a biologic recombinant variant of the endogenous A1M protein, has shown safety and proof-of-mechanism in a Phase 1b study in Cardiac Surgery related Acute Kidney Injury (CS-AKI)

	Overview
Mechanism of Action	**Variant of the endogenous protein A1M** with minor changes to the native amino acid sequence designed to increase solubility and stability • Enhances reduction of oxidative stress, mitochondrial stress, and removal of heme (breakdown product of free hemoglobin) that occurs following ischemic kidney injury • Ischemic kidney injury results from aortic cross-clamping, low blood pressure, hypoperfusion, micro-embolisms & repeat ischemia-reperfusion injury (IRI) during cardio-pulmonary bypass (CPB) • Preclinical data shows Product X reduces proteinuria, plasma creatinine, and blood urea nitrogen while improving renal function in multiple IRI-AKI models • Further, Product X reduced heme-driven kidney injury in rhabdomyolysis and heme-infusion models and protected against cisplatin and radiation induced kidney injury
Phase 2 Study Dosing	• Administered as one IV infusion over 60 minutes 10 minutes before the start of CBP, with four additional doses over 30 minutes 6-, 12-, 24-, and 48-hours following surgery (*5 doses in total*) • Variable start dose based on the patient population: + 1.3 mg/kg if eGFR≥60 mL/min/1.73m² + 0.65 mg/kg in patients with chronic kidney disease (CKD), defined as eGFR<60 mL/min/1.73m²
Efficacy Data-to-Date	• At 6 hours after cardiac surgery in 12 patients (N = 8 with Product X and N = 4 receiving placebo), an exploratory analysis showed Product X led to a reduced postoperative increase in urine biomarkers of tubular stress and injury including: + Liver fatty acid binding protein (L-FABP), neutrophil gelatinase associated lipocalin (NGAL) and NephroCheck® biomarkers (*FDA-approved markers to predict onset of AKI*)
Safety and Pharmacokinetic (PK) Data to Date	• Product X has been used in healthy subjects (N = 36), renally impaired subjects (N = 8), and cardiac surgery patients (N = 8), with **no serious adverse events (SAEs) attributable to the study drug** • Product X has shown a predictable and consistent PK profile with rapid elimination from plasma • Product X is renally cleared and specifically targets proximal tubular cells

Sources: External analysis (draft report, September 2022) & prior work, expert interviews

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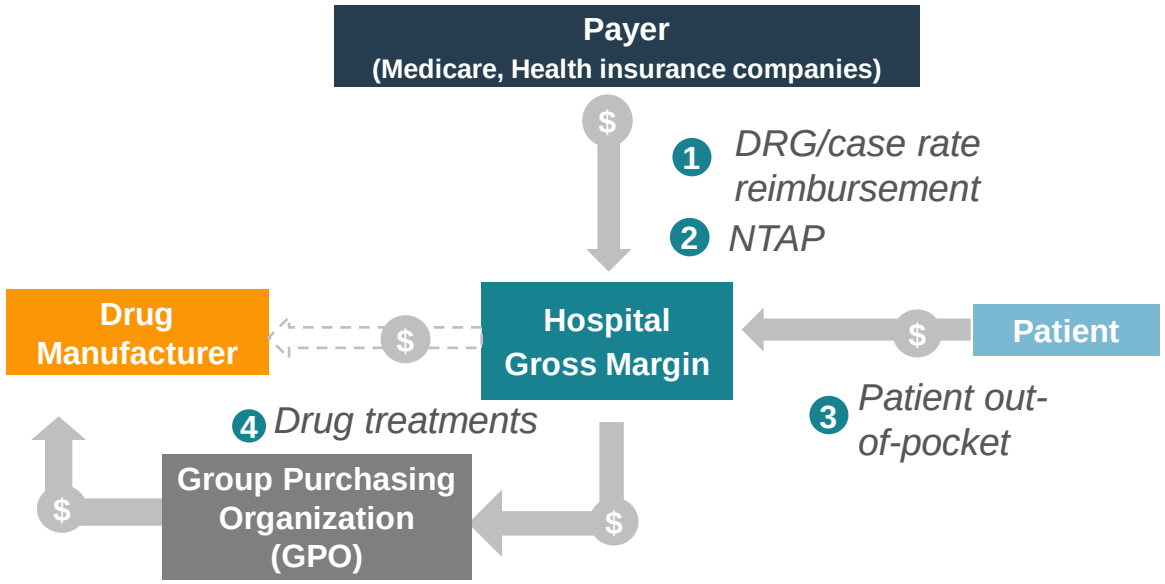
IN-PATIENT HOSPITAL REIMBURSEMENT OF RMC-035 EXPECTED WITHIN A BUNDLED PAYMENT SYSTEM

- Bundled payment for CABG/valve surgery – Diagnosis Related Group (DRG) or case rate
- Hospital margin linked to reimbursement level in DRG system
- Cardiac surgery well reimbursed – provides opportunity to add new therapies

Hospital Reimbursement Landscape



"Coronary artery bypass graft surgery (CABG) ***is one of the top DRG margins for the hospital****"– US Hospital P&T Member*

Sources: External analysis (draft report, September 2022) & prior work

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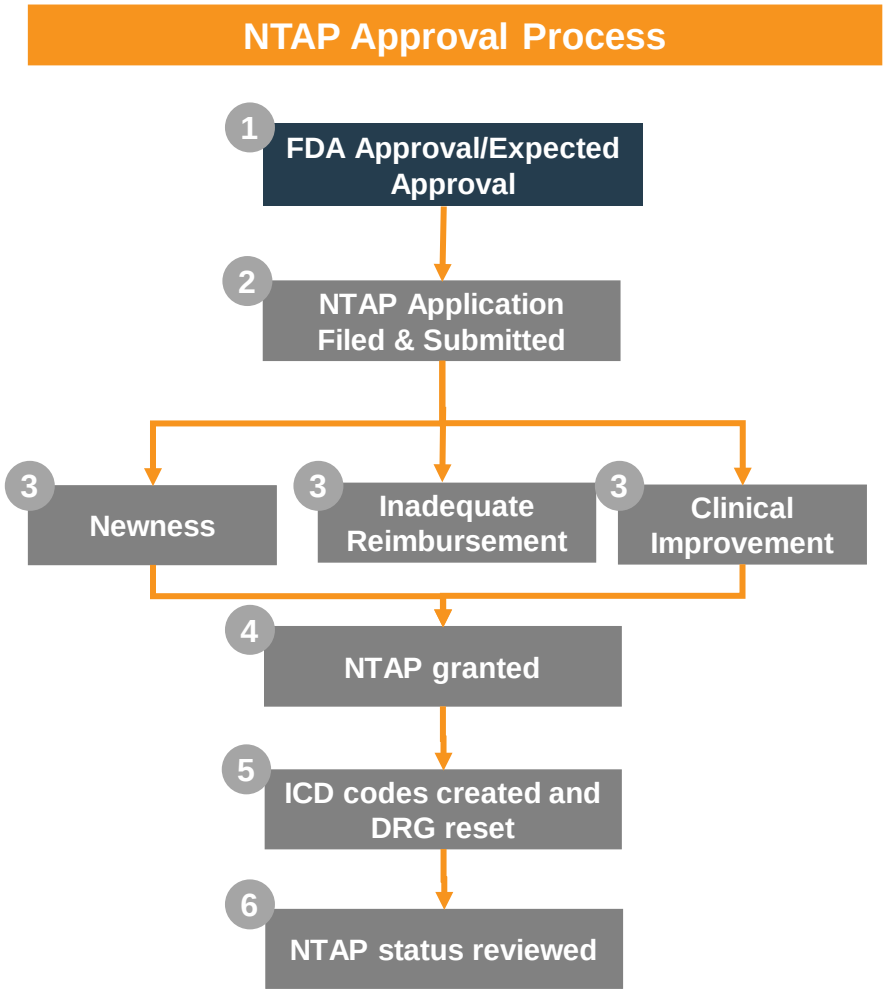
RMC-035 HAS POTENTIAL FOR NTAP

- Intended as a temporary 2-3-year designation, New Technology Add-on Payment (NTAP) status is granted until DRGs are reset

Centers for Medicare & Medicaid Services (CMS) necessitates technologies meet newness, cost, & clinical improvement criteria

- ***Newness*:** Technologies must be approved within the last 2-3 years and are evaluated on relative "newness" through its mechanism of action, DRG coding, and treated patient populations
- ***Inadequate reimbursement:*** Case charges must be >75% above a standard deviation of the Medicare Severity (MS)-DRG case rate
- ***Clinical Improvement:*** Use of the technology must significantly improve clinical outcomes for a specified patient population, compared to currently available treatments



*Centers for Medicare & Medicaid Services; Sources: External analysis (draft report September 2022) & prior work, CMS Policy on New Medical Services and Technologies, FY 2021 Hospital Inpatient PPS Proposed Rule, Manz et al JAMA Netw Open. 2020;3(8):e2012569, Avalere

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METHODOLOGY & APPROACH TO PRICING RESEARCH

- Interviews with stakeholders across US clinical and hospital P&T settings and clinicians with deep experience in management of CS-AKI
  - Covering regional health center, large community hospital, academic medical centers, city hospitals
- Pricing exercises
  - Analogue price value
    - Respondents' perception of price vs clinical value for available analog products
  - Psychological thresholds
    - Unprompted view on acceptable, expensive, and prohibitively expensive price thresholds for RMC-035 treatment
  - Product value
    - Identified clear price points where respondents' perception of price versus clinical value changes from positive to negative

Sources: External analysis (draft report, September 2022)

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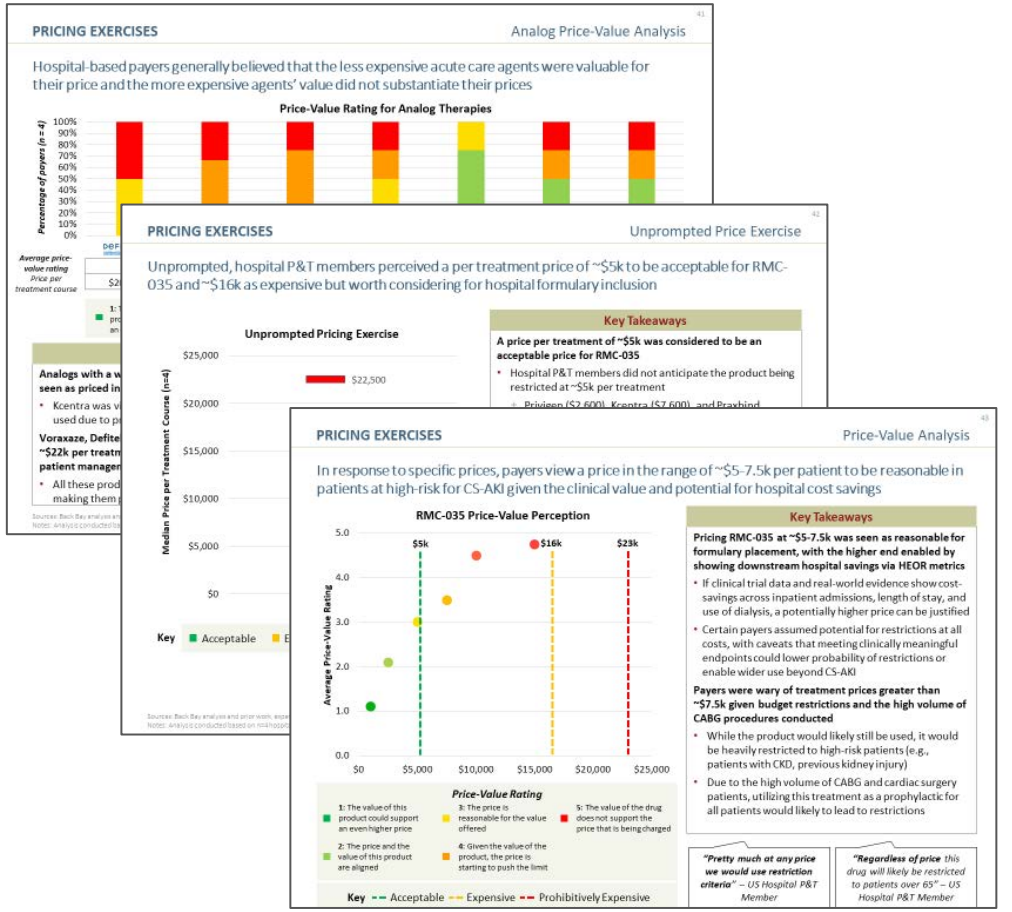
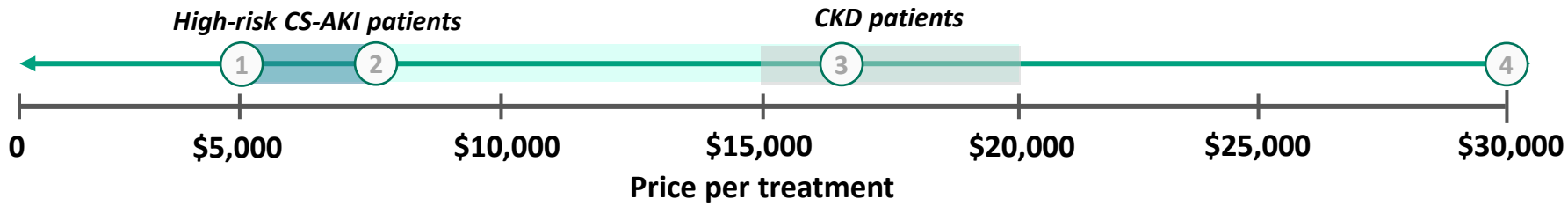
HOSPITAL P&T MEMBERS: ~$5K TO $7.5K PER TREATMENT OF RMC-035 ACCEPTABLE FOR HIGHER RISK PATIENTS (CURRENT TPP)

- Payers benchmarked acceptable pricing to less expensive pricing analogs due to high volume of CABG procedures
  - Analogs with lower price points are more likely to see rapid and generalized uptake in the acute setting
- Unprompted, hospital P&T members perceived a treatment price of ~$5k to $7.5k acceptable per patient
- ~$16k perceived as expensive but still worth considering for hospital formulary inclusion (eg for defined subgroups of patients)



Sources: External analysis (draft report, September 2022) & prior work, expert/P&T member interviews

RATIONALE FOR PRICE RANGE ~$5,000-$20,000 FOR RMC-035, PARTICULARLY IF EVIDENCE FOR DIRECT COST OFFSET OR REDUCTION OF SEVERE RENAL DISEASE



1. **Hospital P&T members did not anticipate the product being restricted at < $7.5k per treatment across patients at high-risk for CS-AKI,** noting the cost per day in the hospital/ICU is $2.5k/$5k and RMC-035 could lead to a direct cost offset

2. ~$7,500/course was seen as the upper pricing limit for RMC-035 assuming that HEOR metrics establish cost-savings for hospitals, with stakeholders also noting **a price greater than ~$7.5k could potentially lead to restrictions**

3. Hospital P&T members perceived a **per treatment price of ~$16k to be expensive but still worth considering for formulary inclusion** given the expense associated with patients who progress to severe renal disease following cardiac surgery. A range of ~$15-20k is potentially acceptable in a more circumscribed population such as patients with CKD.

4. **Angion's ANG-3777 was projected to be priced at ~$30,000 in DGF AKI (**less common than CS-AKI)

Sources: External analysis (draft report, September 2022) & prior work, expert/P&T member interviews

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INITIAL MARKET OPPORTUNITY IN CS-AKI ~$500M-$750M (US ONLY)

- Target patient population is patients who undergo open cardiac surgery (CABG, valve, or combination CABG/valve) at increased risk for CS-AKI
- Total population ~250,000 patients
  - ~160-180,000 CABG with or without valve
  - ~80-100,000 valves (open)
- ~40% of total population fulfil AKI risk criteria
- Addressable patient population ~100,000
- Price potential with current TPP ~$5-7.5k per patient
- Total US addressable market opportunity **~$500M-$750M**
- Global addressable market opportunity in CS-AKI is well above **~$1B**
  - Similar patient numbers in EU5 & US
  - Orphan opportunity in JP

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Sources: External analysis (draft report, September 2022) & prior work, expert/P&T member interviews, clinicaltrials.gov, HCUP 2019, J Thorac Dis. 2018 Mar; 10(3): 1960–1967

SUMMARY & CONCLUSION – US MARKET OPPORTUNITY

- Burden of CS-AKI after cardiac surgery exceeds ~$1B annually (US only)
- In-patient hospital reimbursement for RMC-035 expected via bundled payment
  - CABG surgery well reimbursed – top DRG margins for US hospitals
  - NTAP pathway possible to increase DRG reimbursement level
- Hospital P&T members anticipated price for RMC-035 ~$5k to $7.5k per treatment according to current TPP
  - Evidence for direct cost savings (e.g. length of hospital stay) increases value proposition
- ~$15k to $20k per treatment likely for hospital formulary inclusion in more circumscribed population (e.g. CKD patients)
- US addressable market opportunity in CS-AKI based on current TPP is **~$500M-$750M**
- Global addressable market opportunity in CS-AKI is well above **~$1B**

Significant additional market opportunity with indication expansion

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CONCLUDING REMARKS

TOBIAS AGERVALD, CHIEF EXECUTIVE OFFICER

GUARD THERAPEUTICS INTERNATIONAL AB

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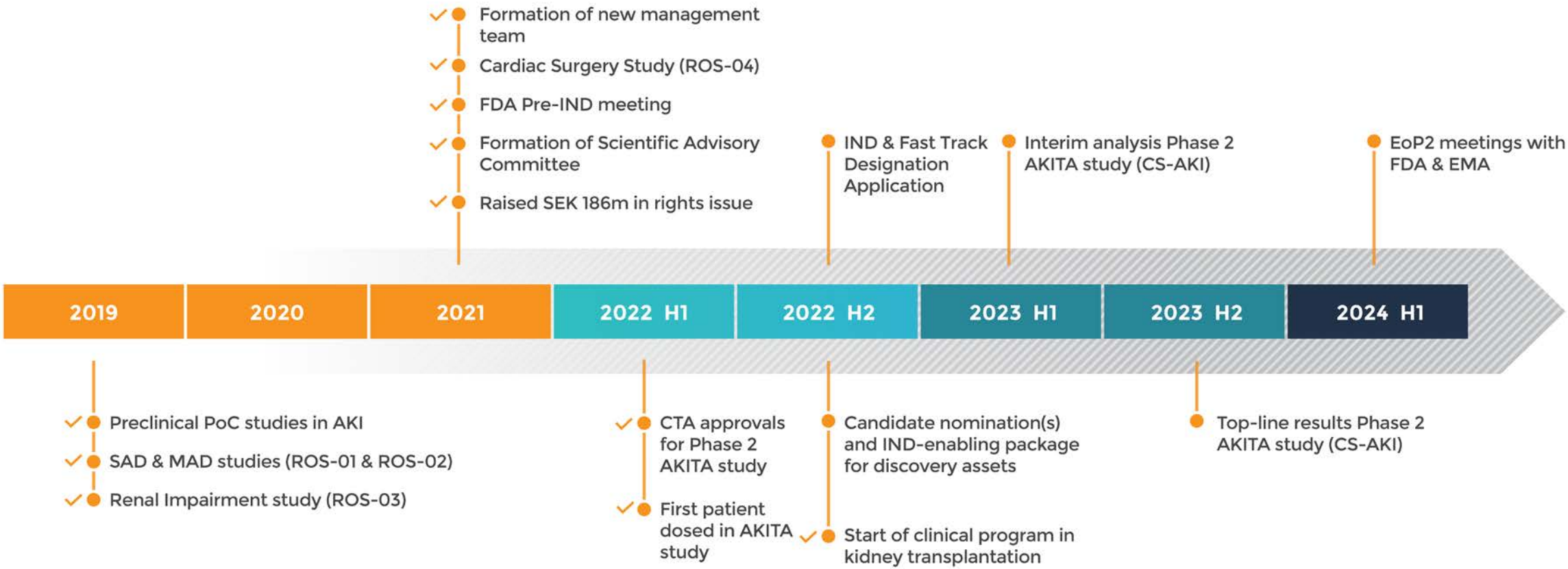
RECENT AND ANTICIPATED NEWS FLOW



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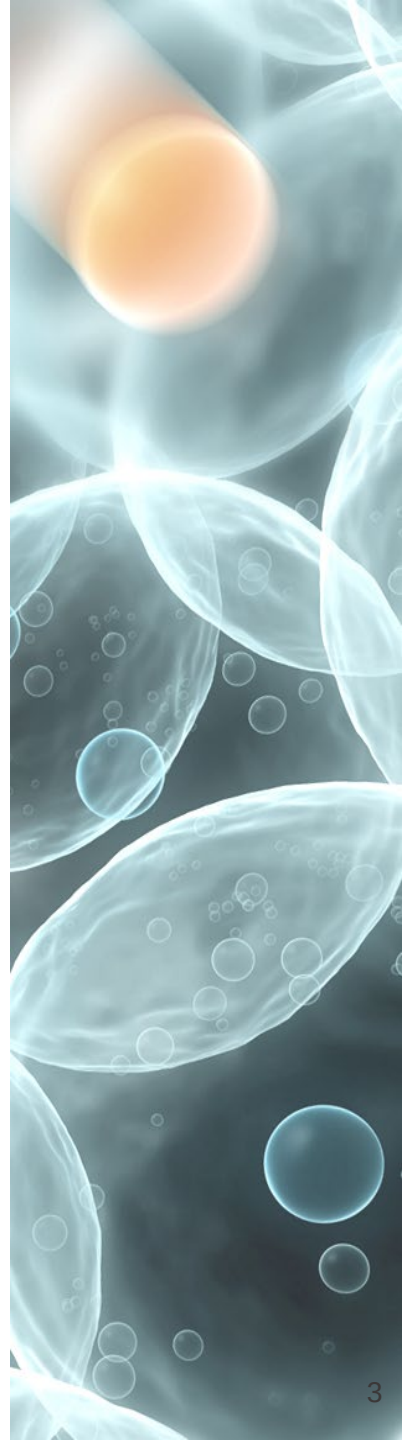
GUARD THERAPEUTICS – KEY HIGHLIGHTS

- ✓ Developing RMC-035, a first-in-class drug for the prevention/early treatment of CS-AKI, a severe and common condition without available therapies
- ✓ Novel mode of action, highly differentiated from competitors, limited competition with high potential to become first-to-market in CS-AKI
- ✓ Addressing significant market opportunity >$1B annually
- ✓ Patent protection until 2037 with potential for further patent extension
- ✓ Strong clinical data in early development with favorable safety profile and biomarker data supportive of kidney cell protection
- ✓ Ongoing large global Phase 2 study (AKITA), recruitment follows projections
- ✓ Significant value inflection points with anticipated interim analysis Q1 2023 and full study results Q4 2023, facilitating design of pivotal study to support NDA/MAA



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Q & A