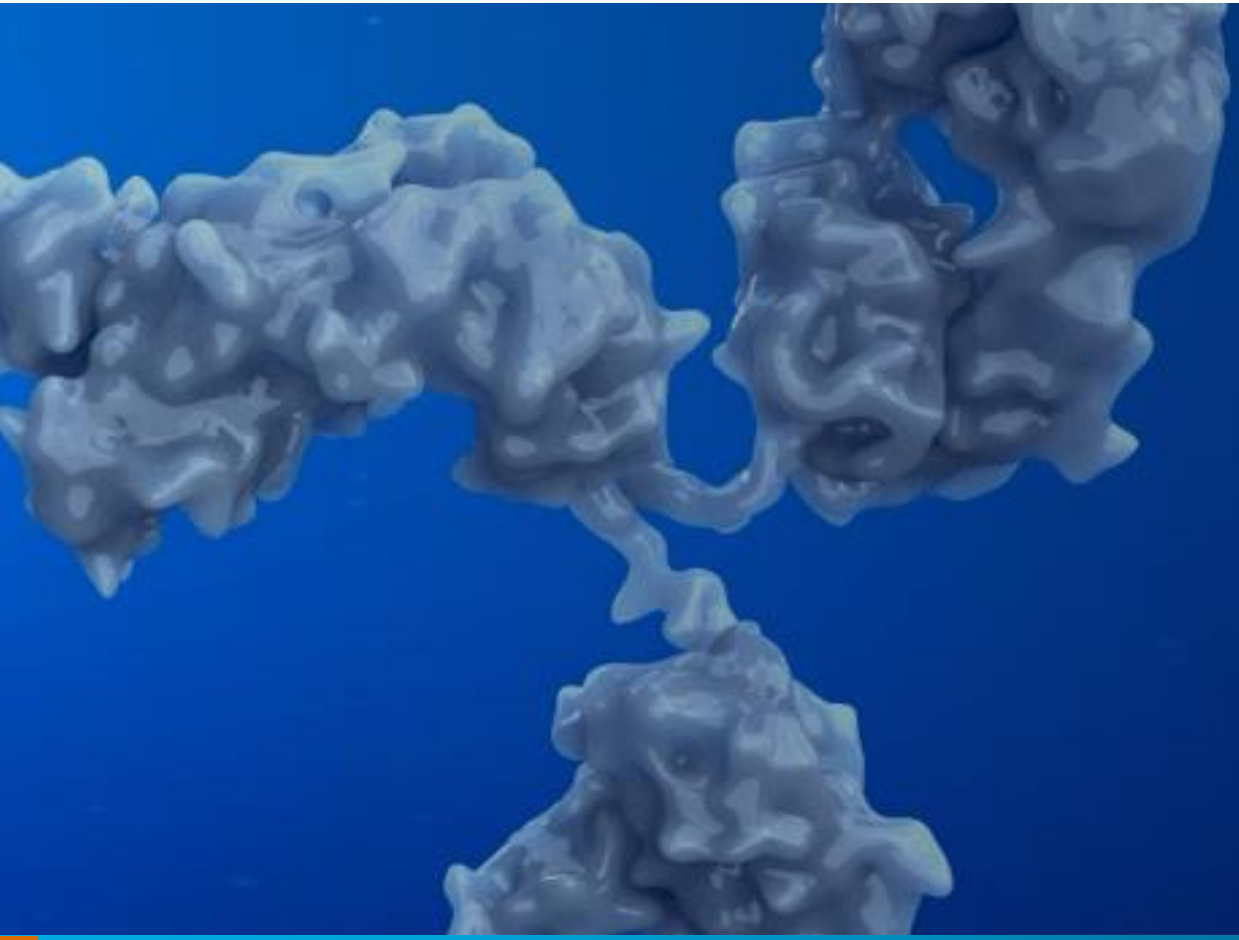


OMEROS®

# J.P. Morgan 39th Annual Healthcare Conference

Gregory A. Demopulos, M.D.
Chairman & Chief Executive Officer
January 13, 2021

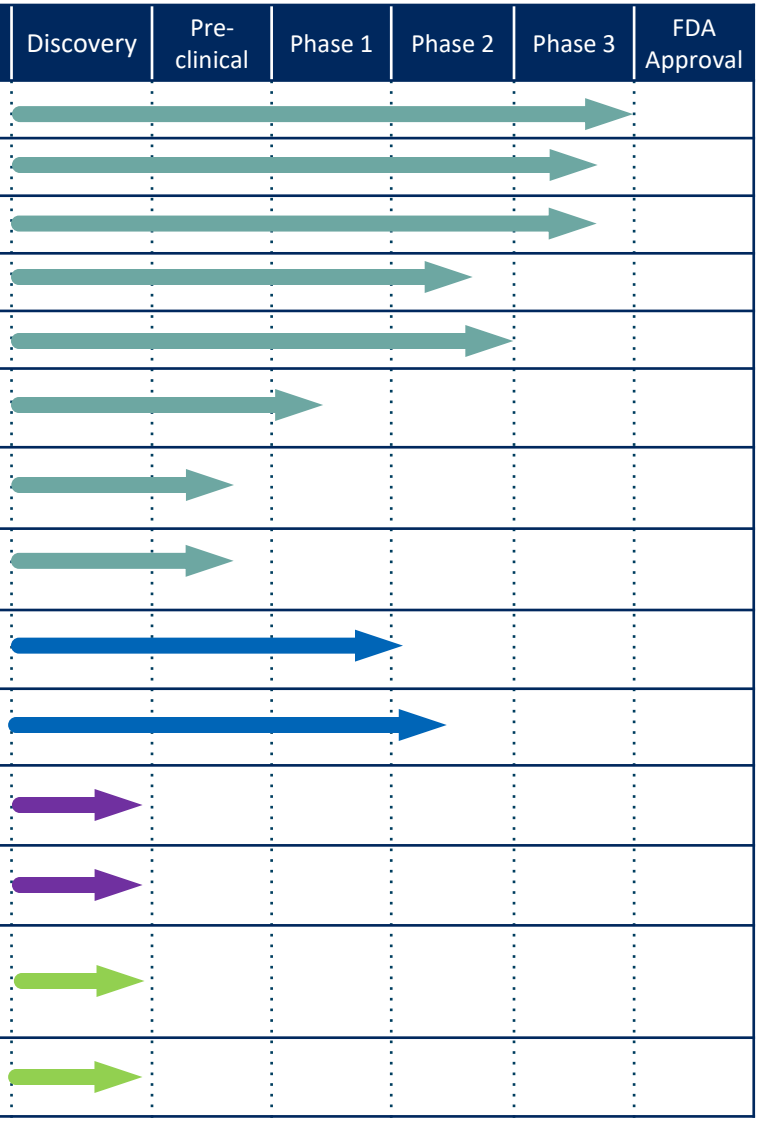
# Safe Harbor

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on the current intent and expectations of the management of Omeros Corporation. These statements are not guarantees of future performance and involve risks and uncertainties that are difficult to predict. Omeros' actual results and the timing and outcome of events may differ materially from those expressed in or implied by the forward-looking statements because of risks associated with Omeros' unproven preclinical and clinical development activities, regulatory oversight, product commercialization, the impact of the COVID-19 pandemic on our business, intellectual property claims, competitive developments, litigation and other factors. For additional information about the factors that affect the company's business, please see the company's latest Forms 10-K and 10-Q filed with the Securities and Exchange Commission. The forward-looking statements made herein are being made as of date of the presentation. Except as required by law, Omeros undertakes no obligation to update any forward-looking statements in this presentation, whether as a result of new information, future events or otherwise.

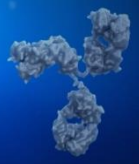
# Highly Diversified Pipeline to Drive Sustainable Growth

*Omeros Controls All Economic Rights Across Its Programs and Platforms*

| | Program / (Candidate) | Molecule | Targeted Disease |
|---|---|---|---|
| Complement Franchise (iCAB) | MASP-2, lectin pathway (narsoplimab (OMS721)) | Ab | Stem Cell Transplant-Associated TMA |
| | | | IgA Nephropathy |
| | | | Atypical Hemolytic Uremic Syndrome |
| | | | Lupus Nephritis & Other Renal Diseases |
| | | | COVID-19 |
| | MASP-3, alternative pathway (OMS906) | Ab | PNH and a Wide Range of Other Alternative Pathway Disorders |
| | MASP-2 (OMS1029) | Ab | Long-Acting 2nd Generation Antibody Targeting Lectin Pathway Disorders |
| | MASP-2, MASP-3, MASP-2/3 | SM | Disorders of the Lectin and Alternative Pathways of Complement |
| Addiction | PDE7 (OMS527) | SM | Addictions and Compulsive Disorders; Movement Disorders |
| | PPARγ (OMS405) | SM | Opioid and Nicotine Addiction |
| Immuno-oncology | GPR174 | SM | Cancer |
| | GPR161 | SM | Cancer |
| Other | GPCR Platform | SM | Immunologic, immuno-oncologic, CNS, Metabolic, CV, Musculoskeletal & Other Disorders |
| | Antibody Platform | Ab | Metabolic, CV, Oncologic, Musculoskeletal & Other Disorders |



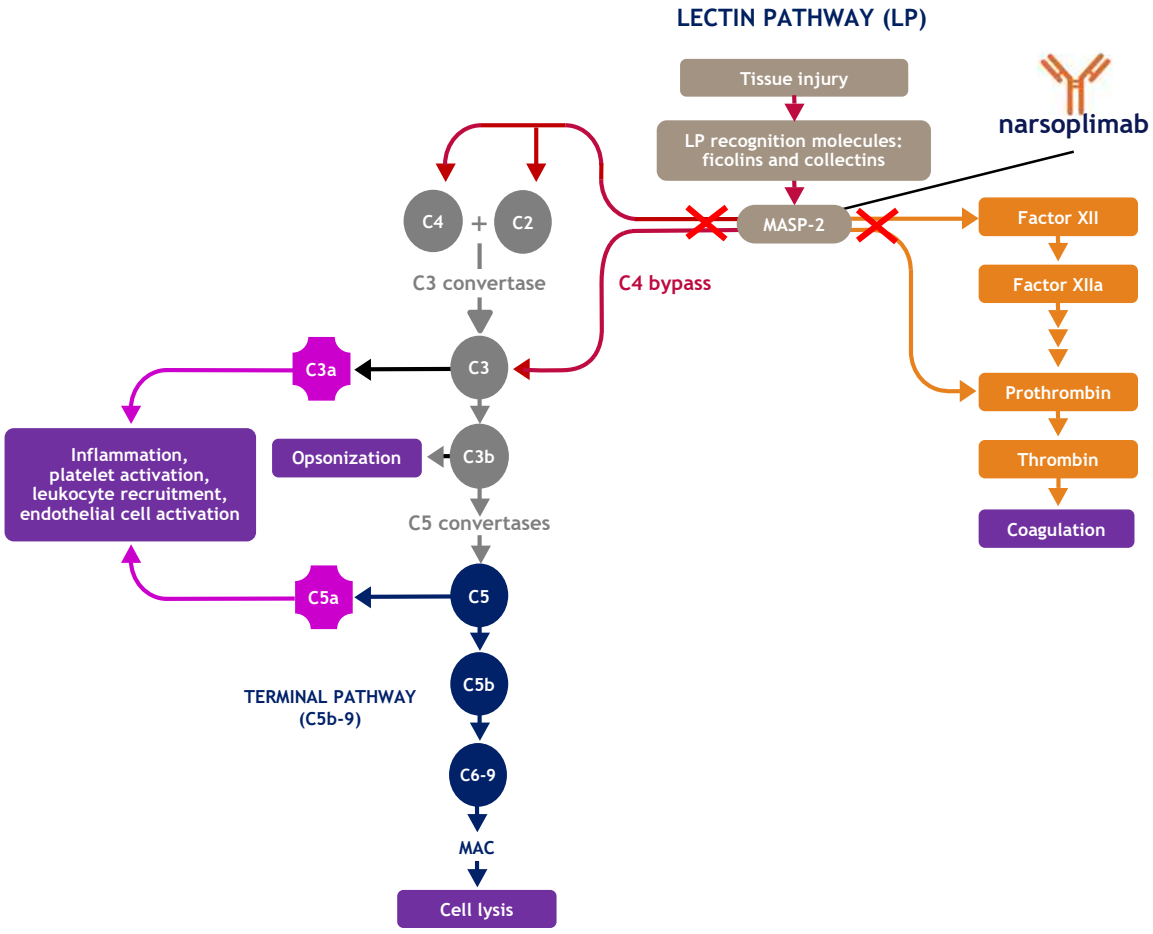
# Narsoplimab – MASP-2 Inhibitor



# Narsoplimab and Regulatory Status

- Narsoplimab is a fully human IgG4 antibody against MASP-2, the effector enzyme of the lectin pathway of complement
- Completed pivotal clinical program in hematopoietic stem cell transplant-associated TMA (HSCT-TMA)
- Completed submission of rolling BLA for HSCT-TMA
- Enrolling 2 additional Phase 3 clinical programs – IgA nephropathy (IgAN) and atypical hemolytic uremic syndrome (aHUS)
- ~250 patients and healthy volunteers have been dosed with narsoplimab
- No significant safety concerns have been observed
- FDA has granted narsoplimab Breakthrough Therapy designation in both HSCT-TMA and IgAN
- Broad therapeutic areas for lectin pathway inhibition:
  - Endothelial injury syndromes
  - Proteinuric diseases
  - Ischemia-reperfusion injury

# Narsoplimab Targets MASP-2 and the Lectin Pathway of Complement




## Narsoplimab

- Fully human monoclonal antibody
- Binds to mannan-binding lectin-associated serine protease-2 (MASP-2), the effector enzyme of the lectin pathway of complement
- Leaves intact the effector function of the adaptive immune response, important for fighting infection
- Blocks MASP-2-mediated coagulation (conversion of prothrombin to thrombin and activation of Factor XII to XIIa) and activation of kallikrein
- Only agent that targets MASP-2 and blocks the lectin pathway

Krarup A et al. 2007. PLoS ONE 2)7): e623; Gulla KC et al. Immunology 2009; 129, 482-495; Demopoulos G et al. W02019246367 (US20200140570A1). World International Property Organization. 26 Dec 2019; Kozarcanin H et al. Journal of Thrombosis and Haemostasis 2016. 14: 531-545.

# Narsoplimab in Hematopoietic Stem Cell Transplant-Associated Thrombotic Microangiopathy

# HSCT-TMA – Serious and Potentially Fatal Complication of HSCT Caused by Endothelial Injury

OMEROS

**25,000 – 30,000**
annual allogeneic HSCT in the US and EU

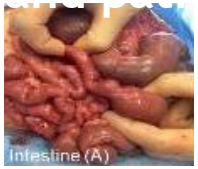
**No approved therapies in HSCT-TMA**

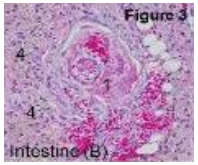

**incidence**
of TMA in allogeneic HSCT


of patients with HSCT-TMA display at least one **high-risk** feature


of severe cases of HSCT-TMA can be **fatal**

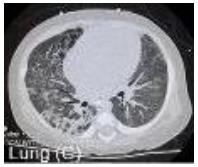
# HSCT-TMA Can Lead to Extended Hospitalizations, Intensive Care Unit Stays and Patient Death

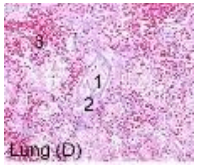



## Intestinal HSCT-TMA (iTMA)

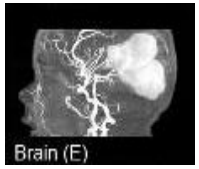
- Ischemic colitis (severe pain)
- Intestinal bleeding
- Histologic TMA features
- Bowel strictures

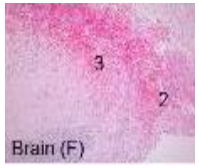



## Pulmonary HSCT-TMA

- Acute hypoxemia (ARDS)
- Interstitial bleeding
- Pulmonary hypertension
- Heart failure




## CNS HSCT-TMA

- Seizures associated with PRES
- CNS bleed
- Hypertension induced
- Endothelial injury



## Skin HSCT-TMA

- Vasculitis
- Purpura
- Vessel thrombosis
- Complement deposits

1. Fibrinoid debris or intravascular thrombus, 2. Denuded endothelial cells, 3. Interstitial hemorrhage, 4. Hemosiderin deposits

Slide used with permission from Sonata Jodele, MD. Jodele S et al. *Blood* Rev. 2015;29(3):191-204. Jodele S et al. *Transfus Apher Sci*. 2016;54(2):181-90.

Dandoy, C et al. Biol Blood Marrow Transplant. 2020. 26(S92); Elfeky, R et al. Blood Adv. 3 June 2020; Vaughn, J et al. Bone Marrow Transplant. 9 November 2018; Li, A et al. Biol Blood Marrow Transplant 2019. 25 (570-576); Roque, A et al. EHA Library May 2019. 268219.

# Narsoplimab In HSCT-TMA: Pivotal Study

## Study Population

- Single-arm, open-label study of high-risk HSCT-TMA patients
- Protocol specified that patients receive narsoplimab once weekly for ≥ 4 weeks
- 93% of the trial population had multiple risk factors for poor outcomes

| Demographics | N=28 |
|---|---|
| Mean & median age (years) | 48 |
| Male Gender, n (%) | 20 (71.4%) |
| Malignant underlying disease | 27 (96.4%) |
| Risk factors: | |
| Presence of GVHD, n (%) | 19 (67.9%) |
| Significant infection, n (%) | 24 (85.7%) |
| Pulmonary dysfunction (%) | 5 (17.9%) |
| Neurological dysfunction, n (%) | 16 (57.1%) |
| Renal dysfunction | 21 (75.0%) |
| Multi-organ involvement, n (%) | 14 (50.0%) |

## Efficacy Measures

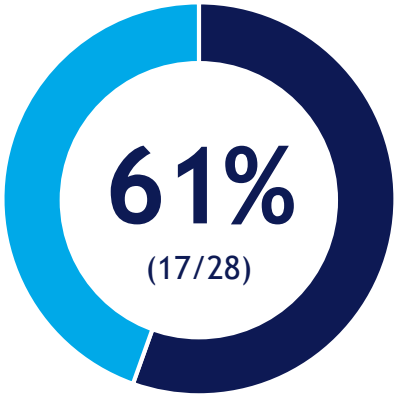
- **Primary Endpoint:** Response as assessed by clinically meaningful improvement in TMA laboratory markers and organ function
  - ***15% complete response rate is the FDA-agreed threshold for primary endpoint***
- **Secondary Endpoints:** 100-day survival and change from baseline in TMA lab measures

## Key Findings

- Most narsoplimab-treated patients achieved a complete response, exceeding the targeted threshold for the primary efficacy endpoint
- 100-day survival was similarly impressive across all groups (responders, per-protocol, and intent-to-treat)
- Narsoplimab was well tolerated in this very sick population with multiple comorbidities
- No safety signal observed: observed adverse events were comparable to those typically seen in post-transplant population
- 21% of patients died during the trial due to causes common in HSCT

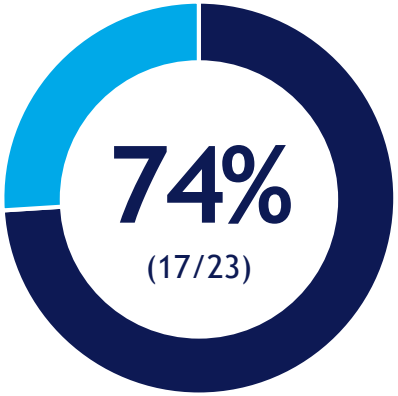
# Complete Response Rates (%)

**All treated patients (N=28)**
(95% CI)




(40.6% to 78.5%)
p<0.0001*

**Patients treated per protocol (≥ 4 weeks of dosing) (n=23)**
(95% CI)




(51.6% to 89.8%)
p<0.0001*

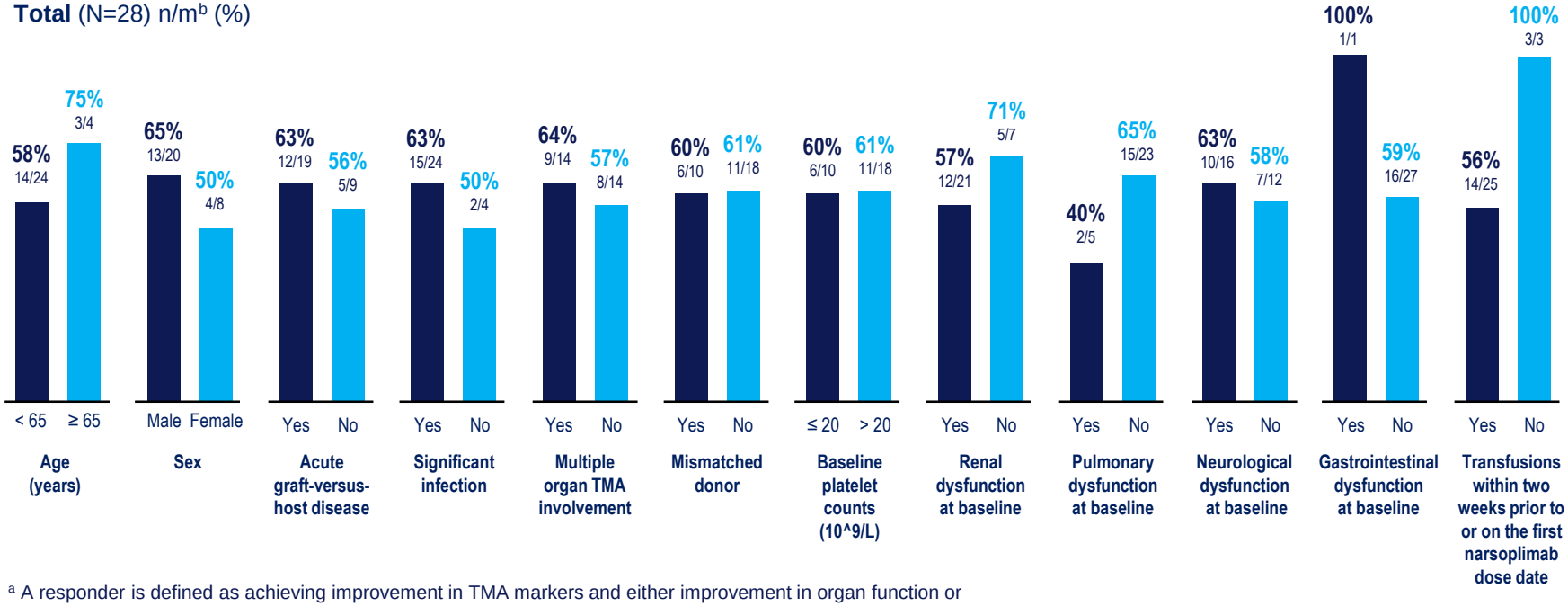
- 15% is the FDA-agreed efficacy threshold for the primary endpoint (i.e., the complete response rate) in the clinical trial

* Exact two-sided p-value for testing response rate equal to 15%

# Complete Response by Subgroup (%)

## Responders[a]

**Total** (N=28) n/m[b] (%)



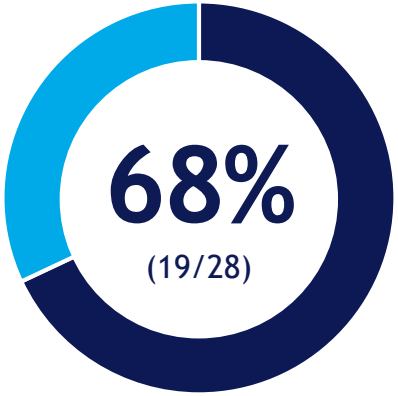

[a] A responder is defined as achieving improvement in TMA markers and either improvement in organ function or freedom from transfusion. Patients whose response cannot be determined are considered non-responders.

[b] m is the number of patients in the corresponding subgroup.

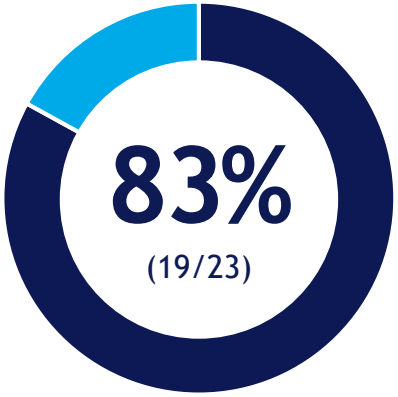
OMS721-TMA-001. A Phase 2 Trial. Data on file; Rambaldi A et al. EHA Library. June 15, 2018. Abstract nr PF724; Rambaldi, A et al. European Hematology Society. Abstract S262. 2020.

# 100-Day Survival Following HSCT-TMA Diagnosis

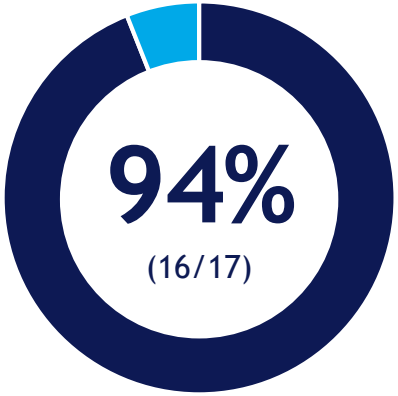
**All treated patients (N=28)**




**Patients treated per protocol (≥ 4 weeks of dosing) (n=23)**




**Complete responders (n=17)**



# Patient Survival with Narsoplimab

## Kaplan-Meier Plot of Overall Survival for HSCT-TMA

**Median survival for the full analysis population was 274 days**

(95% CI) (103, NE)

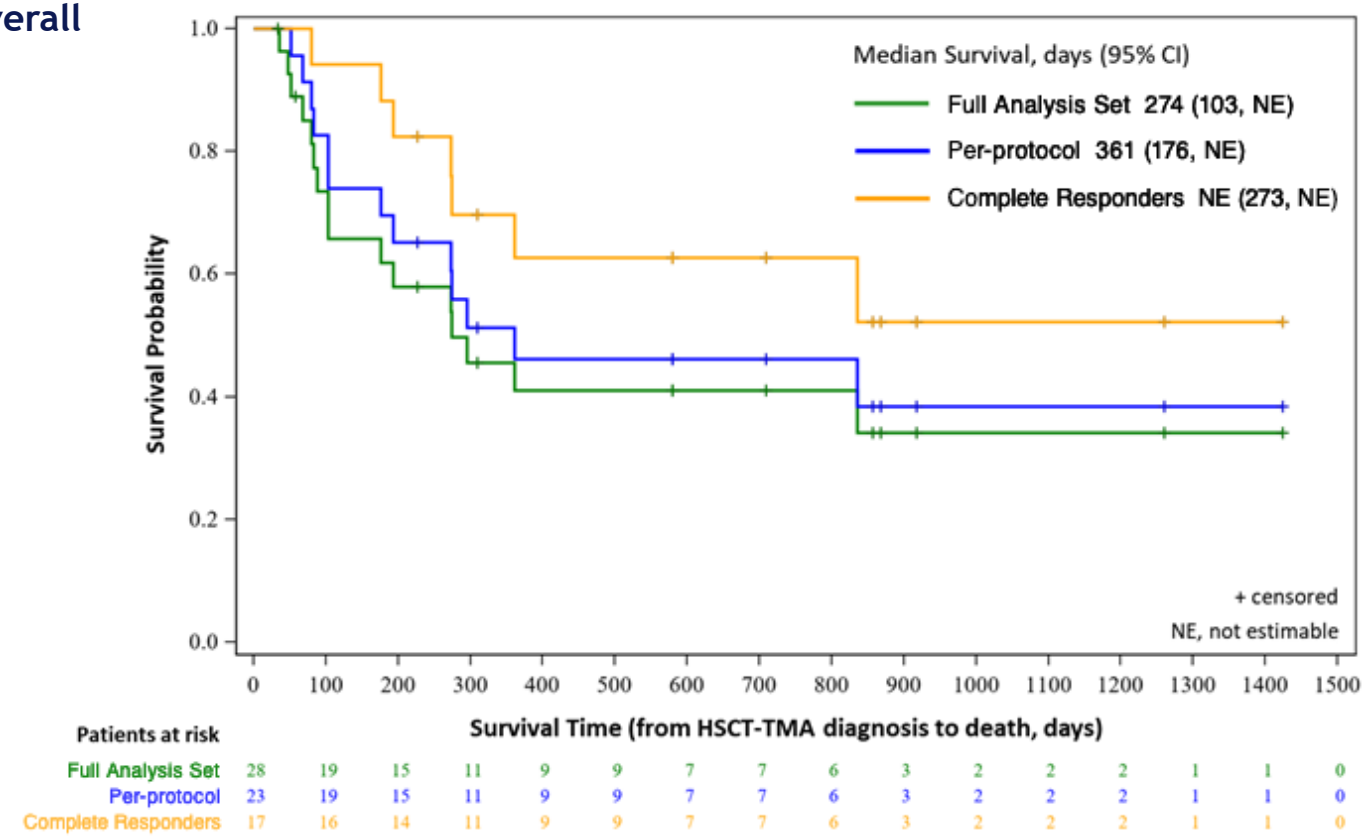
**Median survival for the per-protocol population was 361 days**

(95% CI) (176, NE)

**Median survival for the responder population was not estimable**

(95% CI) (273, NE)

Median survival is estimated by Kaplan-Meier method. 95% confidence interval for median survival is calculated using complementary log-log transformation.



# Safety and Tolerability: Most Common Adverse Events in >15% of Patients

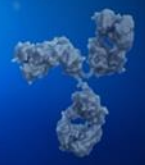
- Narsoplimab was well tolerated in this very sick population with multiple comorbidities
- The most commonly reported adverse events were nausea, vomiting, diarrhea, hypokalemia, neutropenia and fever
- The observed adverse events are comparable to those typically seen in the post-transplant population
- 6 patients died during the trial due to causes common in HSCT

| Preferred Term, n (%) | (N = 28) |
|---|---|
| Any Event | 27 (96.4) |
| Pyrexia | 10 (35.7) |
| Diarrhea | 9 (32.1) |
| Vomiting | 9 (32.1) |
| Nausea | 7 (25.0) |
| Neutropenia | 7 (25.0) |
| Fatigue | 6 (21.4) |
| Hypokalemia | 6 (21.4) |
| Back pain | 5 (17.9) |

# Regulatory and CMC Milestones for Narsoplimab in HSCT-TMA

## Narsoplimab in HSCT-TMA: Moving Rapidly Toward Global Regulatory Approvals

- Breakthrough therapy designation from FDA
- Orphan Drug designation from FDA and from EMA
- BLA under review by FDA – submitted mid-November
- MAA submission is in preparation for submission to EMA; targeting 1H 2021 for completion
- Drug substance and drug product process validation lots successfully completed
- More than sufficient supply of drug product for launch



# Narsoplimab in HSCT-TMA
# Launch Readiness Milestones

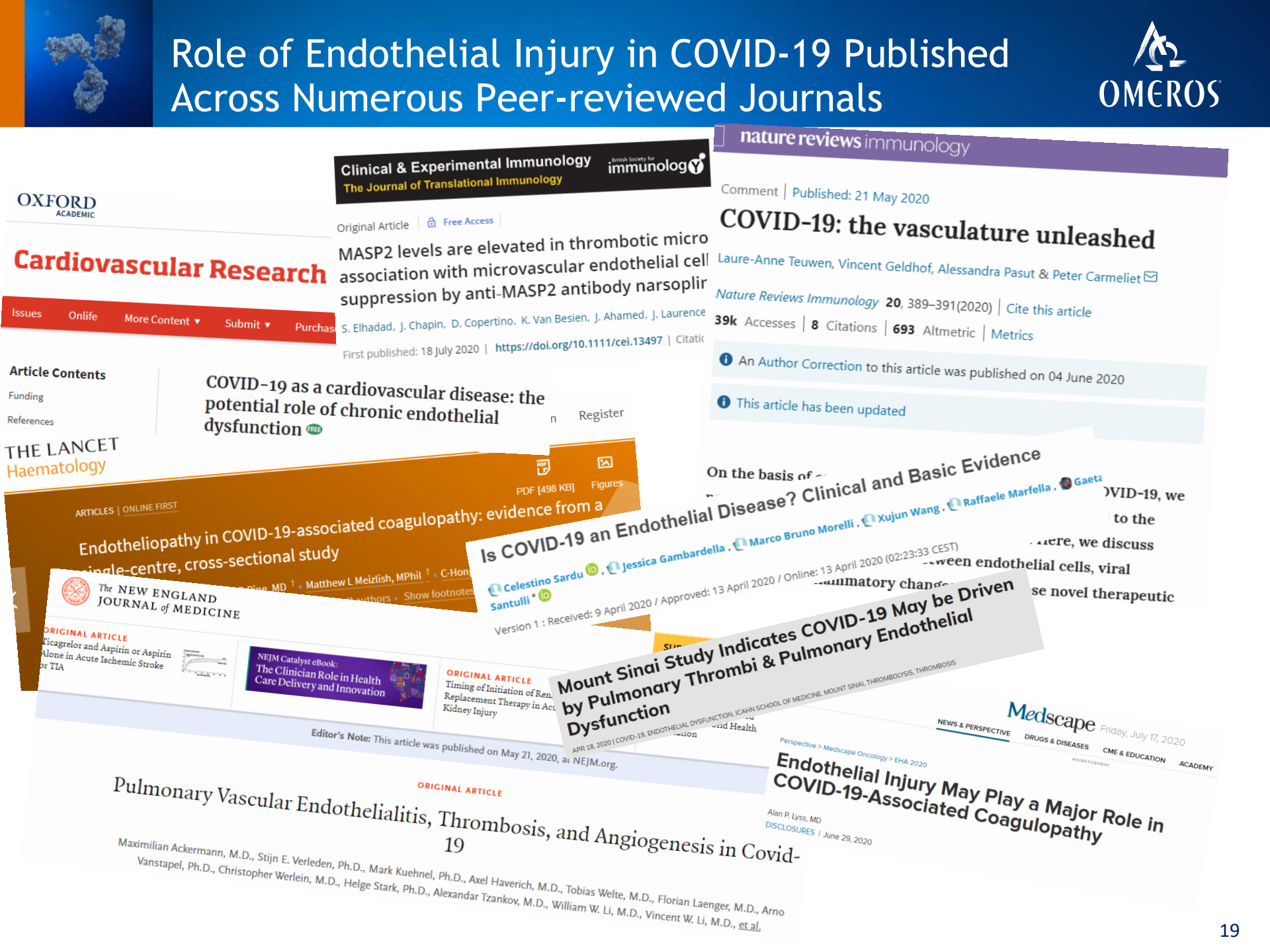
OMEROS

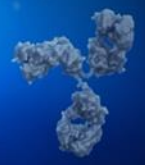
| | |
|---|---|
| **Engagement** | Comprehensive engagement plan with top leaders from US and international transplant centers<br>✓ Introduce Omeros as a potential new partner in the transplant market<br>✓ Increase awareness of HSCT-TMA<br>✓ External steering committee establishing guidelines for diagnosis and treatment |
| **Education** | ✓ Initiation of educational disease awareness campaign focusing on HSCT-TMA pathogenesis and unmet need<br>✓ International digital and print campaign<br>✓ Significant 2020 presence at US/EU hematology and transplant congresses |
| **Value** | Robust value framework to demonstrate clinical and financial value to global payers and providers<br>✓ Pricing strategy to ensure broad access across provider segments<br>✓ HEOR/RWE plan – reduction in post-HSCT complication costs; improved outcomes<br>✓ Convenient route of administration in inpatient and outpatient settings<br>✓ Pursuing coding strategy to ensure seamless access to narsoplimab, if approved (ICD-10, NTAP, J-code, etc.) |
| **Operations** | Organizational launch readiness<br>✓ Heads of national sales, medical science liaisons and advocacy already hired<br>✓ US Sales force hiring process initiated<br>✓ Long-term commercial manufacturing agreement with Lonza executed<br>✓ Commercial lots successfully manufactured |

# Narsoplimab for the Treatment of COVID-19-related ARDS Requiring Mechanical Ventilation

# Role of Endothelial Injury in COVID-19 Published Across Numerous Peer-reviewed Journals

OMEROS





# Endothelial Injury with Complement Activation is Central to Pathophysiology of HSCT-TMA and COVID-19

OMEROS

- Once endothelial injury occurs, pathophysiology of HSCT-TMA and COVID-19 are similar
- Endothelial injury activates the lectin pathway of complement
- In HSCT-TMA, endothelial injury is caused by conditioning regimen, immunosuppressants, GVHD and infection
- In COVID-19, endothelial injury is caused by direct viral infection
- MASP-2, the lectin pathway's effector enzyme, is bound by the nucleocapsid and spike proteins of SARS-CoV-2, activating the lectin pathway that leads to amplification of underlying cellular injury and induces cytokine response
- Viral load has no correlation in COVID-19 patients to clinical status or disease severity

***Components of COVID-19:***

- ***Complement activation***
- ***Inflammation***
- ***Coagulation***

} ***Narsoplimab inhibits all 3***

# Parallels Between COVID-19 and HSCT-TMA

| Comparator | COVID-19 | HSCT-TMA |
|---|---|---|
| Lectin-Pathway Activation from Endothelial Damage | ✓ | ✓ |
| Cause of Endothelial Injury | Viral | Conditioning regimen, Immunosuppressants, GVHD, infection |
| MASP-2 Activation | ✓ | ✓ |
| Multi-Organ TMA | ✓ | ✓ |

- ~70 patients have been dosed with narsoplimab across the two endothelial injury syndromes

# Data from Cohort 1 of the COVID-19 Study in Italy[1]

OMEROS

## Demographics and Treatment Summary

| Demographic | Median (range) or n (%) |
|---|---|
| **Age** | 57 years (47-63) |
| **Male sex** | 5 (83%) |
| **Weight** | 86 Kg (82-100 Kg) |
| **Comorbidities** | Diabetes (n=1); Hypertension (n=1); Dyslipidemia (n=2); Obese/Overweight (n=6) |

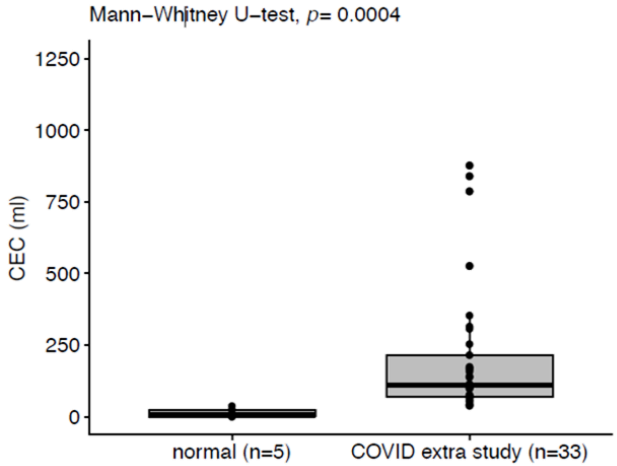
| Treatment Summary | n (%) or Median (range) |
|---|---|
| **Timing of narsoplimab treatment from start of CPAP oxygen support** | |
| ***Within 24 hours*** | 4 (67%) |
| ***Within 48 hours*** | 2 (33%) |
| **Time from hospital admission to treatment** | 2 days (1-4) |
| **Duration of follow-up (to date) after first dose** | 27 days (16-90) |

All patients recovered, survived and were discharged – 2 retrospective control groups with similar entry criteria and baseline characteristics had mortality rates of 32% and 53%

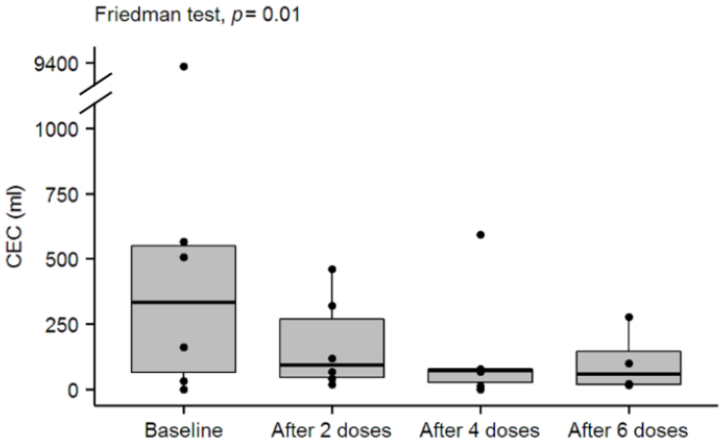
[1]Rambaldi, A. et al. Endothelial injury and thrombotic microangiopathy in COVID-19: treatment with the lectin-pathway inhibitor narsoplimab. *Immunobiology* https://doi.org/10.1016/j.imbio.2020.152001 (2020).

# Data from Cohort 1 of the COVID-19 Study in Italy

## Evidence of Endothelial Damage (CEC Counts) in COVID-19

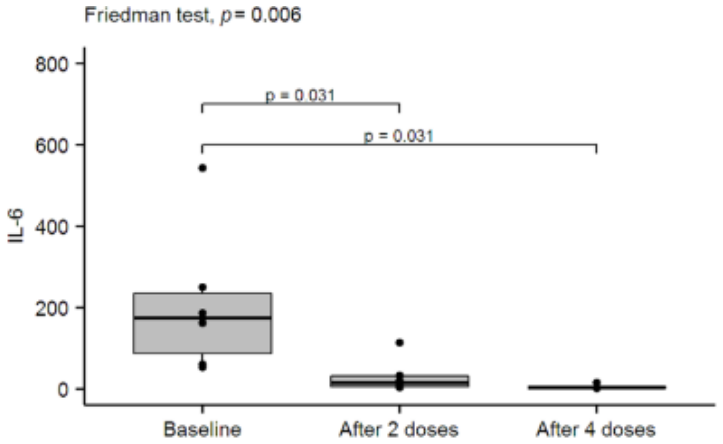


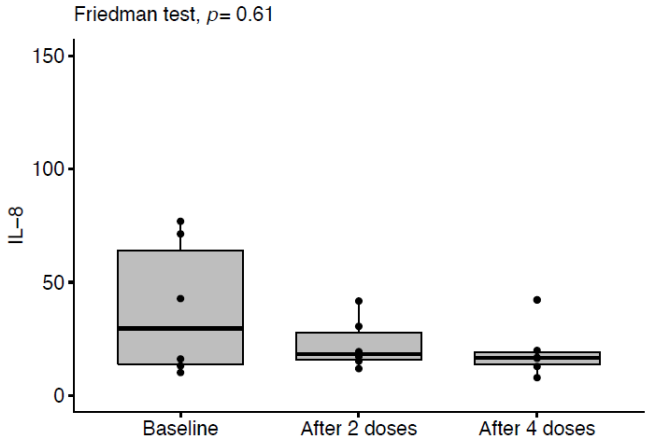

*5 normal (uninfected) and 33 infected patients without Narsoplimab*




*6 infected patients treated with Narsoplimab*

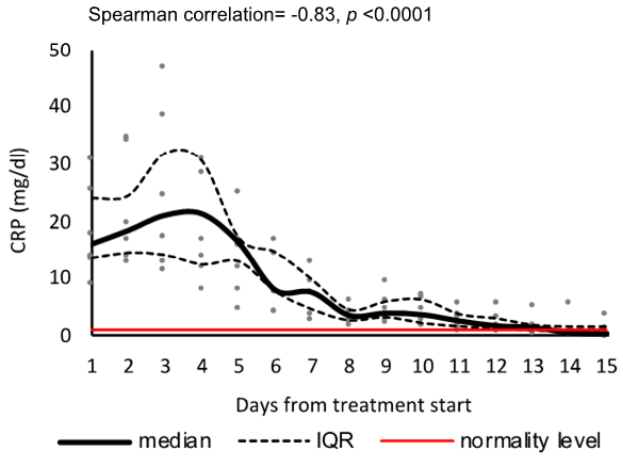
## IL-6 / IL-8 Levels Improved in all 6 Patients Treated with Narsoplimab



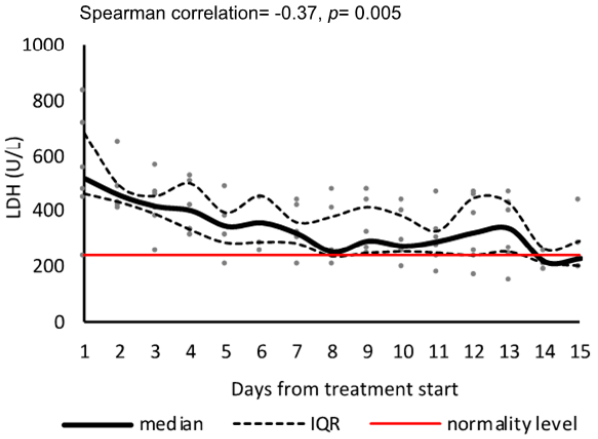



# Data from Narsoplimab-treated COVID-19 Patients

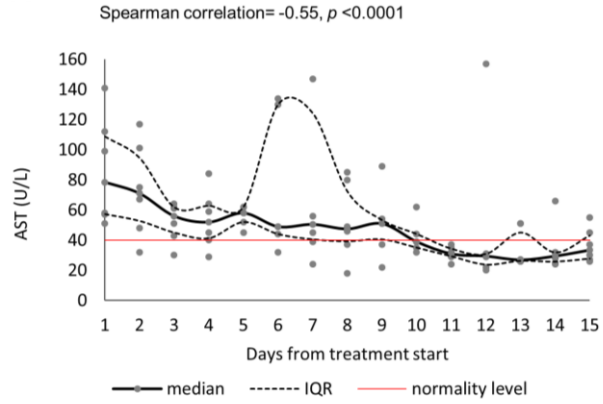
## C-Reactive Protein Improved in all 6 Patients



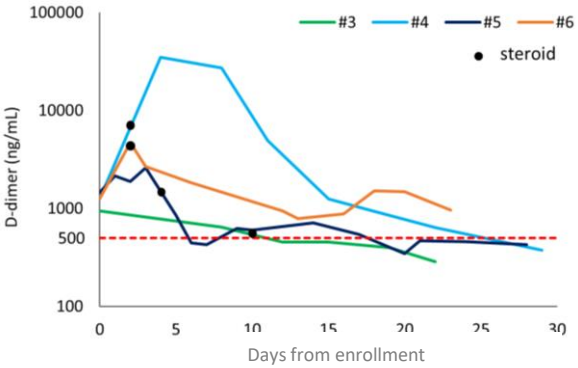

## Lactate Dehydrogenase Improved in all 6 Patients




## Aspartate Aminotransferase (AST) Improved in all 6 Patients



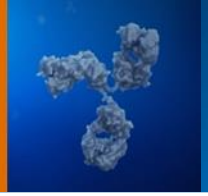

## D-Dimer Improved in all Assessed Patients



# Narsoplimab Could Have a Role in Treatment of "Long-Hauler" COVID-19 Patients

- Published studies from multiple international research groups now show that "recovered" COVID-19 patients have high incidence of longer-term sequelae – e.g., cognitive impairment/CNS, cardiac, pulmonary, multi-organ disorders

- COVID-19 patients treated with narsoplimab show no observed clinical or laboratory evidence of sequelae at 5-6 months after treatment

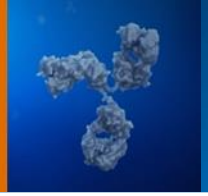


# At 5-6 Month Follow-Up, All Cohort 1 Patients Are Without Clinical or Laboratory Evidence of Sequelae

OMEROS

| Laboratory Findings | Baseline | Last Evaluation (5-6 Mos. Post-Discharge) |
|---|---|---|
| White cell count - per $mm^3$, median (range) | 8335 (6420-10,120) | 7320 (3200-8770) |
| > 10,000 per $mm^3$ - no. (%) | 2 (33) | 0 (0) |
| < 4000 per $mm^3$ - no. (%) | 0 (0) | 1 (17) |
| Lymphocyte count - per $mm^3$, median (range) | 875 (410-1290) | 2815 (810-3780) |
| Platelet count - x $10^3$ per $mm^3$, median (range) | 282 (199 -390) | 238 (170-354) |
| Hemoglobin - g/dL, median (range) | 13.4 (13.2-14.1) | 14.8 (13.4-15.8) |
| Distribution of other findings (laboratory reference ranges) | | |
| C-reactive protein (0.0-1.0 mg/dL) | 14 (9.5-31.3) | 0.15 (0-0.5) |
| Lactate dehydrogenase (120/246 U/L) | 518.5 (238-841) | 212 (119-249) |
| Aspartate aminotransferase (13-40 U/L) | 78.5 (51-141) | 18 (12-29) |
| Alanine aminotransferase (7-40 U/L) | 73 (37-183) | 22.5 (20-67) |
| Creatinine (0.3-1.3 mg/dL) | 0.85 (0.38-1.33) | 0.94 (0.51-1.07) |
| D-dimer (< 500 ng/mL) | | |
| < 190 - no. (%) | 0 (0) | 3 (50) |
| > 190 - median (range) | 1250.5 (943-1454) | 324 (202-390) |

**Clinical status at last evaluation of all 6 patients – no evidence of COVID sequelae**



# Experience with Narsoplimab Following Initial Cohort of Bergamo Patients

OMEROS

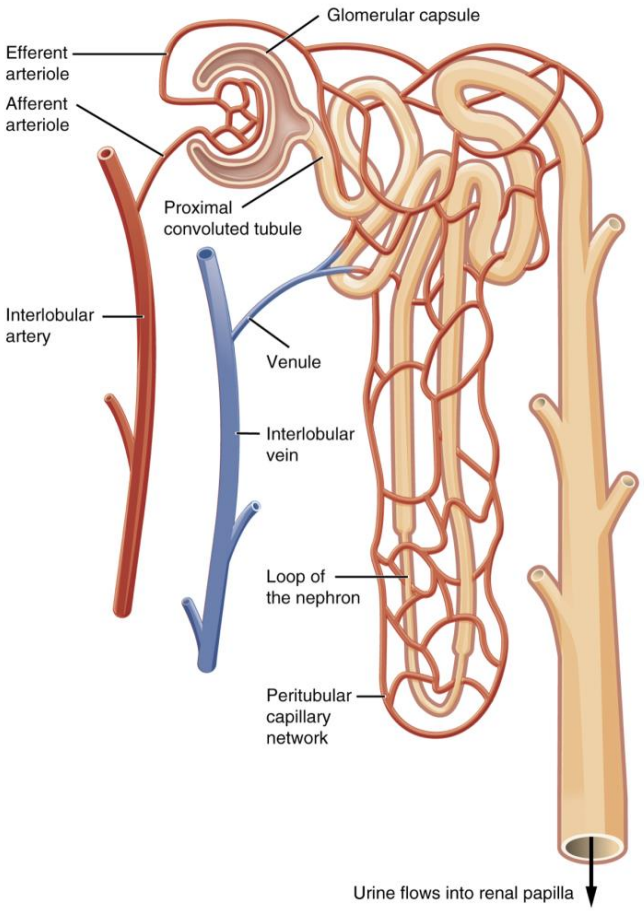
- Have continued treating patients in the US and in Bergamo under compassionate use
  - All additional patients have been severely ill prior to treatment with narsoplimab
    - All intubated with majority initiating narsoplimab multiple days after intubation
    - All had failed other therapies prior to initiating narsoplimab
  - Similarly striking outcomes to those in the initial Bergamo study

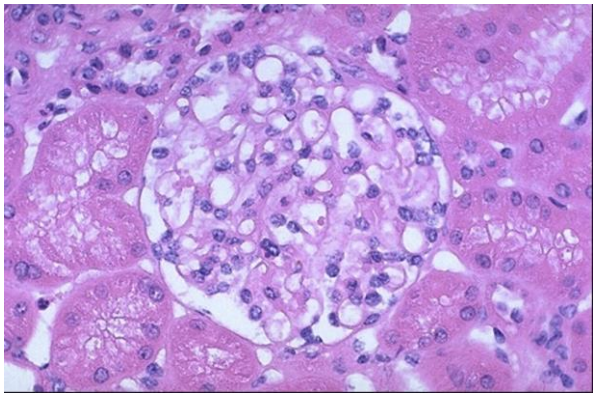
- COVID-19 patients treated with narsoplimab develop appropriately high anti-SARS-CoV-2 antibodies
- Advancing discussions with BARDA, NIAID, NCATS and the Biden-Harris Transition COVID-19 Advisory Board
- In discussions with international regulatory authorities regarding narsoplimab for COVID-19
- Now part of the I-SPY COVID-19 TRIAL: An Adaptive Platform Trial for Critically Ill Patients

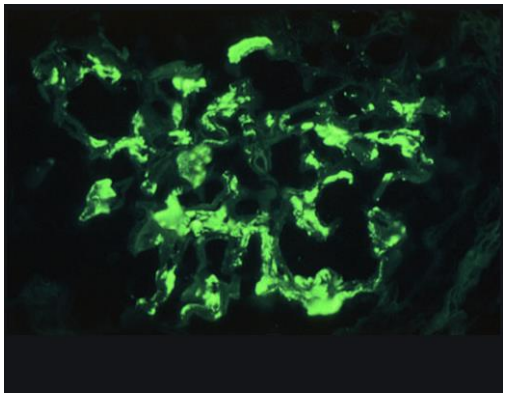
OMEROS

# Narsoplimab in IgA Nephropathy

# Role of Lectin Pathway in IgAN





Nephrol Dial Transplant (1999) 14: 881–886

Nephrology Dialysis Transplantation

*Original Article*

**Glomerular deposition of mannose-binding lectin in human glomerulonephritis**

Karl Lhotta[1], Reinhard Würzner[2] and Paul König[1]

Nephrol Dial Transplant (1998) 13: 1984–1990

Nephrology Dialysis Transplantation

*Original Article*

**Glomerular deposition of mannose-binding lectin (MBL) indicates a novel mechanism of complement activation in IgA nephropathy**

Morito Endo[1], Hiroyuki Ohi[1], Isao Ohsawa[1], Takayuki Fujita[1], Misao Matsushita[2] and Teizo Fujita[2]

**Mesangial IgA2 Deposits and Lectin Pathway–Mediated Complement Activation in IgA Glomerulonephritis**

Satoshi Hisano, MD, Misao Matsushita, PhD, Teizo Fujita, MD, Yuzo Endo, MD, and Shigeo Takebayashi, MD

Article

**Mesangial C4d Deposits in Early IgA Nephropathy**

*Alfons Segarra,[1] Katheryne Romero,[1] Irene Agraz,[1] Natalia Ramos,[1] Alvaro Madrid,[2] Clara Carnicer,[3] Elias Jatem,[4] Ramón Vilalta,[2] Luis Enrique Lara,[2] Elena Ostos,[4] Naiara Valtierra,[4] Juliana Jaramillo,[1] Karla V. Arredondo,[1] Gema Ariceta,[5] and Cristina Martínez[1]*

NEPHRON

Original Paper

Nephron 1998;80:408–413

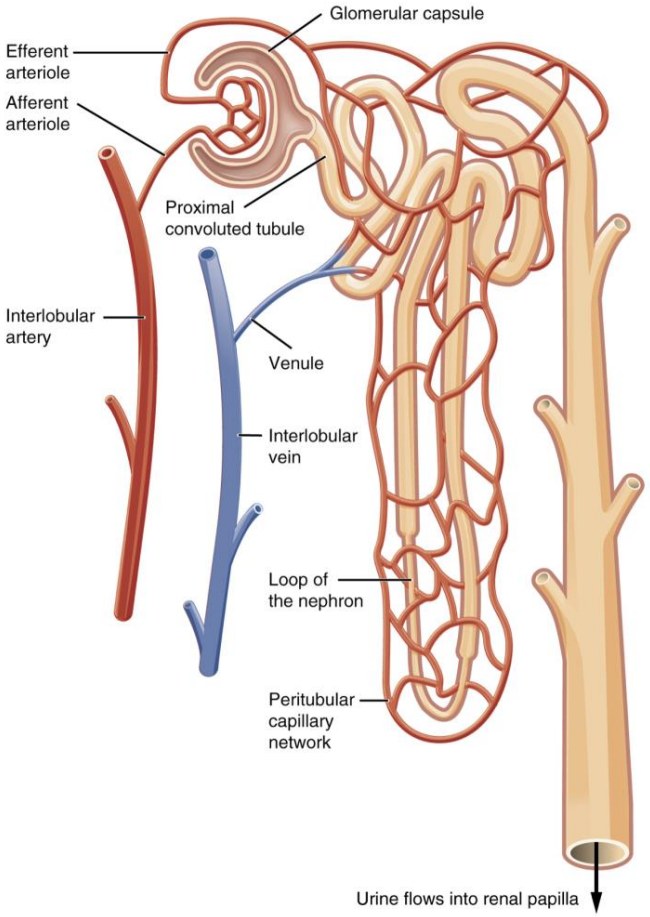
Accepted: June 26, 1998

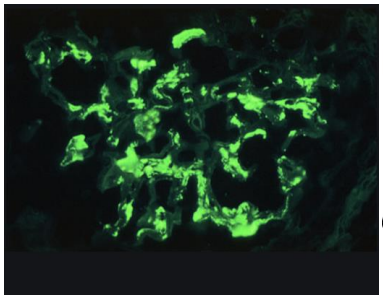
*Mitsuhiro Matsuda[a]*
*Kenichi Shikata[a]*
*Jun Wada[a]*
*Hikaru Sugimoto[a]*
*Yasushi Shikata[a]*
*Toshisuke Kawasaki[b]*
*Hirofumi Makino[a]*

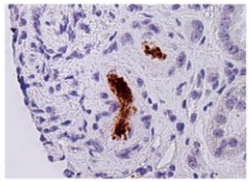
[a] Department of Medicine III, Okayama University Medical School, Okayama, and [b] Department of Biological Chemistry, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan

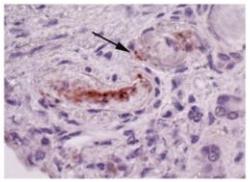
**Deposition of Mannan Binding Protein and Mannan Binding Protein-Mediated Complement Activation in the Glomeruli of Patients with IgA Nephropathy**

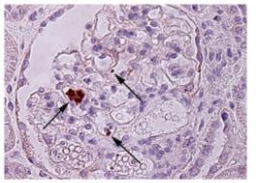
# Thrombotic Microangiopathy and IgAN

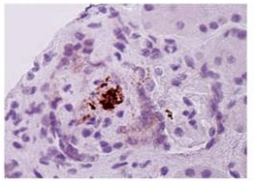








CLINICAL RESEARCH www.jasn.org

**A Clinicopathologic Study of Thrombotic Microangiopathy in IgA Nephropathy**

Khalil El Karoui,*† Gary S. Hill,* Alexandre Karras,‡ Christian Jacquot,‡ Luc Moulonguet,§ Olivier Kourilsky,‖ Véronique Frémeaux-Bacchi,¶ Michel Delahousse,** Jean-Paul Duong Van Huyen,* Alexandre Loupy,* Patrick Bruneval,* and Dominique Nochy*

*Department of Pathology, Hôpital Européen Georges Pompidou, Paris, France; †Institut National de la Santé et de la Recherche Médicale INSERM U845, Hôpital Necker-Enfants Malades, Paris, France; ‡Department of Nephrology, Hôpital Européen Georges Pompidou, Paris, France; §Department of Nephrology, Hôpital Ambroise Paré, Boulogne Billancourt, France; ‖Department of Nephrology, Hôpital Sud Francilien, Evry, France; ¶Department of Immunology, Hôpital Européen Georges Pompidou, Paris, France; and **Department of Nephrology, Hôpital Foch, Suresnes, France

Nephrol Dial Transplant (2019) 1–6
doi: 10.1093/ndt/gfz241

ndt Nephrology Dialysis Transplantation

**Glomerular endothelial activation, C4d deposits and microangiopathy in immunoglobulin A nephropathy**

Hernán Trimarchi[1] and Rosanna Coppo[2]

[1]Nephrology Service, Hospital Británico de Buenos Aires, Buenos Aires, Argentina and [2]Fondazione Ricerca Molinette, Regina Margherita Hospital, Turin, Italy

REVIEW

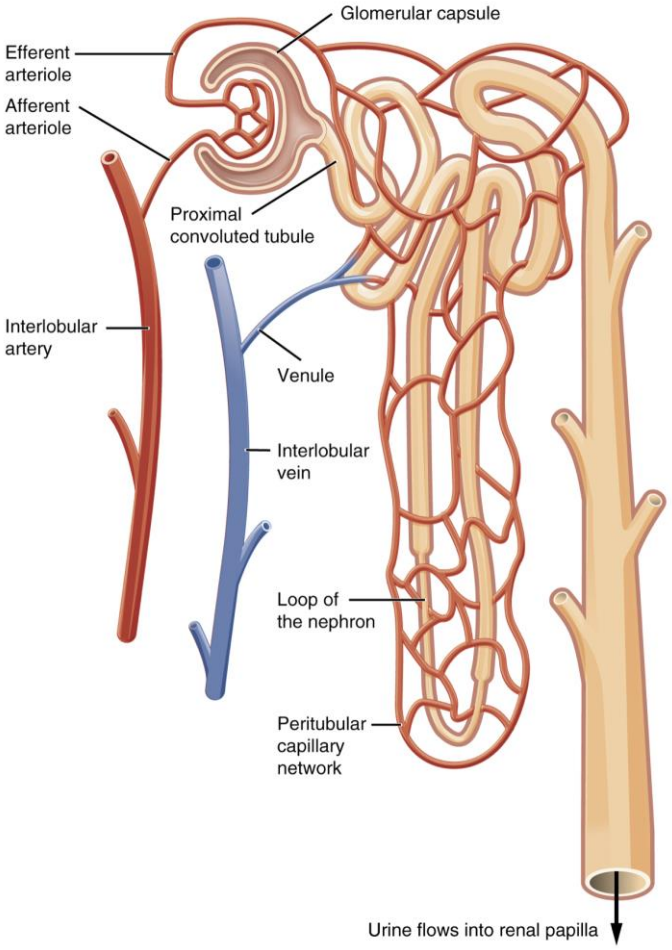
KI REPORTS KIReports.org CLINICAL RESEARCH

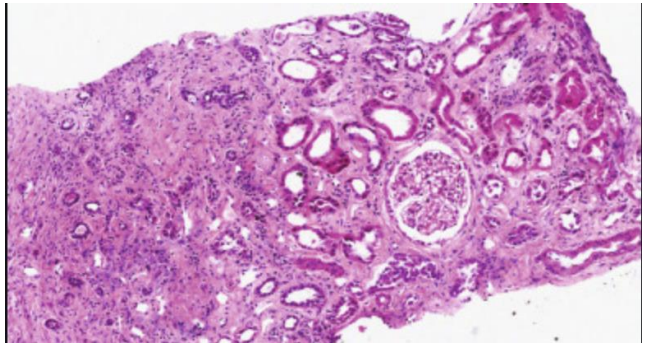
**Epidemiology and Pathophysiology of Glomerular C4d Staining in Native Kidney Biopsies**

Cinthia B. Drachenberg[1], John C. Papadimitriou[1], Preeti Chandra[2], Abdolreza Haririan[2], Susan Mendley[3], Matthew R. Weir[2] and Mario F. Rubin[2]

[1]Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland, USA; [2]Department of Medicine, Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland, USA; and [3]Department of Pediatrics, Division of Nephrology, University of Maryland School of Medicine, Baltimore, Maryland, USA

# Tubulointerstitial Fibrosis in IgAN




frontiers in Immunology

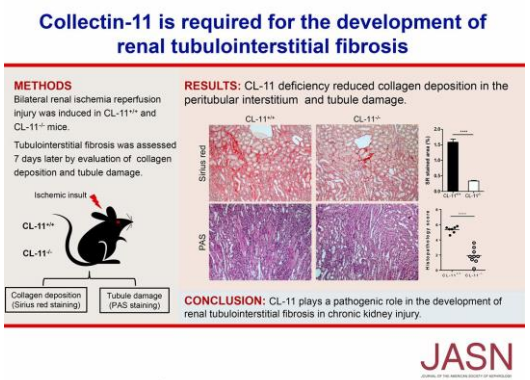
ORIGINAL RESEARCH

Absence of the Lectin Activation Pathway of Complement Ameliorates Proteinuria-Induced Renal Injury


frontiers in Immunology

HYPOTHESIS AND THEORY

Collectin-11 (CL-11) Is a Major Sentinel at Epithelial Surfaces and Key Pattern Recognition Molecule in Complement-Mediated Ischaemic Injury



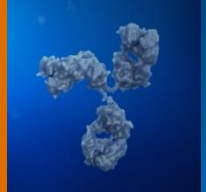
# Narsoplimab Clinical Program in IgAN

## Phase 2 Clinical Trial

- Substudy 1: Narsoplimab in patients with IgAN, lupus nephritis, C3 glomerulopathy and membranous nephritis, all who were receiving treatment with corticosteroids
- Substudy 2: Narsoplimab in patients with IgAN who were not receiving corticosteroids

## Phase 2 Trial Results

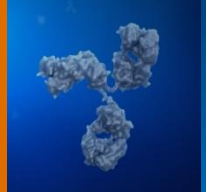
- Across the 2 studies, median proteinuria reduction was 60-70% and eGFR stabilized
- 4 of 5 lupus nephritis patients showed ~70% decrease in 24-hour urine protein
- No treatment-related serious adverse events (SAEs) were observed
- Manuscripts published
  - J. Barratt and R. Lafayette, *MASP-2 inhibition as a potential strategy for the management of IgA nephropathy,* Drugs of the Future 2020, 45(6): 389-396
  - R. Lafayette, et. al., *Safety, Tolerability, and Effect of Narsoplimab (OMS721), a Novel MASP-2 Inhibitor for the Treatment of IgA Nephropathy,* Kidney International Reports 2020, 5(11), 2032-2041



# Summary of ARTEMIS-IGAN Phase 3 Trial – Enrolling at over 100 Sites Globally

OMEROS

| | |
|---|---|
| **Overview** | • Phase 3 randomized, double-blind, placebo-controlled trial of narsoplimab in patients with IgA nephropathy<br>• Planned enrollment primary endpoint = 280 patients (140/arm)<br>  ➢ High-Risk Subset (≥2g UPE) = 156 patients (78/arm) |
| **Inclusion Criteria** | • Biopsy-confirmed diagnosis of IgAN within 8 years prior to screening<br>• Proteinuria of >1 g/day within 6 months prior to screening or uPCR >0.75 by spot urine at screening<br>• Mean of two proteinuria measurements >1 g/day at baseline<br>• eGFR of ≥ 30mL/min/1.73 $m^2$ at screening and baseline |
| **Efficacy Measures** | • Primary efficacy endpoint: Change from baseline 24-hour urine protein excretion (UPE g/day) at 36 weeks from baseline for **EITHER** the entire population or the subset of "high-protein" spillers<br>• Secondary efficacy endpoints include rate of change from baseline in eGFR |



# Regulatory Milestones for Narsoplimab in IgAN

OMEROS

**Narsoplimab: Advancing Toward Global Regulatory Submissions in IgAN**

- Breakthrough Therapy designation from FDA
- Orphan Drug designation from FDA and from EMA
- First and only IgAN investigational treatment to receive breakthrough therapy designation
- Potential to seek full or accelerated approval on proteinuria alone in either of the overall or high-protein-spiller populations
- Over 100 trial sites activated and enrolling for Phase 3 trial in US, EU, Australia, Canada and Asia; additional sites being activated
- Enrollment challenging due, in good part, to COVID-19 – working to add sites in China but data read-out will be delayed beyond 2021

OMEROS

# OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3%

# OMIDRIA®
# Ophthalmological Surgery

OMEROS

- First and only FDA-approved intraocular product to prevent miosis and to reduce postoperative ocular pain in both adult and pediatric patients
- Used in over 1 million cataract procedures without any safety concerns
- Strong post-launch (“real-world”) clinical data
- On VA National Formulary and continuing to expand reimbursement across commercial and Medicare Advantage payers
- Issued patents through 2033 (2035 if pending patents issue)
- Nearly 4 million cataract procedures performed annually in US
- Permanent J-code
- Separate payment in ASCs
- NOPAIN Act introduced in House and Senate with broad and growing bipartisan co-sponsorship and leadership/committee-member support
- Net sales in 3Q 2020 were $34.8 million prior to an $8.7 million return reserve in connection with expiration of pass-through on October 1, 2020

# Real-World Evidence — OMIDRIA® Improves Outcomes

OMEROS

Peer-reviewed publications detailing post-launch studies demonstrate that the use of OMIDRIA statistically significantly:

- ✓ Prevented IFIS[1]
- ✓ Prevented iris prolapse[1]

***Compared to steroids:****

- ✓ Reduced cystoid macular edema[2,3]
- ✓ Decreased breakthrough iritis[3]
- ✓ Reduced pain[3]

***Compared to epinephrine:***

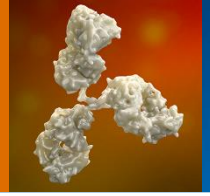
- ✓ Decreased complication rates[4]
- ✓ Decreased use of pupil-expanding devices[4-8]
- ✓ Enabled performance of surgery and postoperative care without the use of steroids[2,3,9]
- ✓ Shortened surgical times[4,6,8]
- ✓ Reduced need for opioids (*i.e.*, fentanyl) during surgery while decreasing VAS pain scores[10]
- ✓ Prevented miosis during femtosecond laser-assisted surgery[7]
- ✓ Improved uncorrected visual acuity on day after surgery[4]

*OMIDRIA used intraoperatively with postoperative NSAIDs (no steroids) when compared to postoperative steroids with or without NSAIDs (no OMIDRIA)

1. Silverstein SM, et al. J Cataract Refract Surg. 2018;44(9):1103–1108. 2. Walter K, et al. J Cataract Refract Surg. 2020;46:350–354. 3. Visco DM, et al. Effect of intracameral phenylephrine and ketorolac 1.0%/0.3% on postoperative cystoid macular edema, iritis, pain, and photophobia following cataract surgery. J Cataract Refract Surg. In press. 2020. 4. Rosenberg ED, et al. Clin Ophthalmology. 2018;12:21–28. 5. Bucci FA, et al. Clin Ophthalmology. 2017;11:1039–1043. 6. Visco D. Clin Ophthalmol. 2018;12:301–305. 7. Walter K, et al. J Cataract Refract Surg. 2019;45(4):465-469. 8. Data on file. Clinical outcomes of phenylephrine/ketorolac intraocular solution versus epinephrine in cataract surgery in a real-world setting. 9. Al-Hashimi S, et al. J Cataract Refract Surg. 2018;44:1032–1041. 10. Donnenfeld, E et al. Clin Ophthalmol. 2019;13:2143-2150.

OMEROS

# MASP-3 Development Program



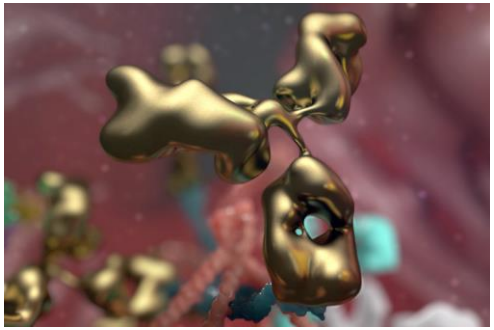
# OMS906 Inhibits MASP-3, Considered the Premier Target in the Alternative Pathway

OMEROS

- MASP-3 is the key activator of the alternative pathway ("AP")
- MASP-3 is the premier target within the AP
  - Has the lowest concentration of all AP proteins
  - Has low relative clearance of AP targets
    - Example: ~50% of systemic CFD is cleared per hour
  - Unlike C5 and C3 blockers, leaves intact the lytic arm of the classical pathway, important in fighting infection

# Properties of OMS906

## OMS906



Humanized monoclonal antibody **highly potent** and **selective** for MASP-3

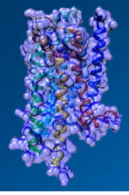
## Infrequent SubQ Administration

Convenient dosing regimen allows self-administration in an **outpatient setting**

OMS906
is designed to treat multiple alternative pathway-driven diseases with infrequent, SubQ delivery

Initial Phase 1 clinical data expected later this year

# G-Protein Coupled Receptors (GPCR) Platform



# Immuno-Oncology: GPR174

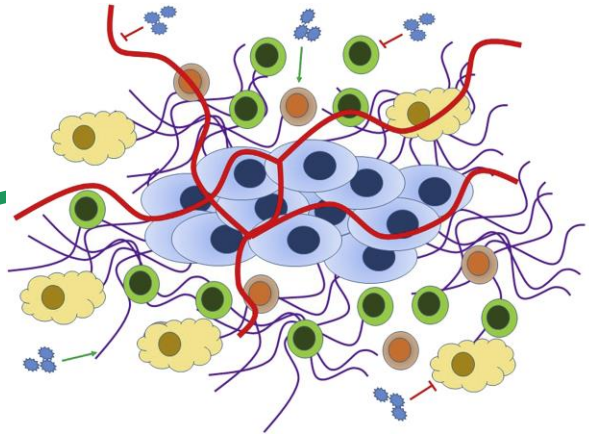
- GPR174 inhibition amplifies tumor-killing properties of T and NK cells
- GPR174 is activated by phosphatidylserine (PS) and lyso PS, which are produced by the tumor microenvironment, especially following chemo- or radiation therapy
- GPR174 inhibitors have the potential to address non-responders to current therapies
  - Combined inhibition of GPR174 and the adenosine pathway synergistically enhanced anticancer phenotypes
  - GPR174 inhibition may be amenable to combination with checkpoint inhibitors, cellular therapies and cytotoxic therapies
- GPR174 is expressed almost exclusively in the immune system

# Activating Ligands for GPR174 and Adenosine Receptors A2A/A2B Are Products of the Tumor Microenvironment

OMEROS

## Cell stress and death in the tumor microenvironment

PS & lysoPS are abundant in tumors
- From tumor cells, exosomes & extracellular vesicles, immune cells, platelets, vascular endothelium
- Further enriched by chemo- and radiation-therapy




ATP → CD39 → CD73 → Adenosine

PS & LysoPS → GPR174 → Gαs → cAMP

Adenosine → A2A/A2B → Gαs → cAMP

T cell

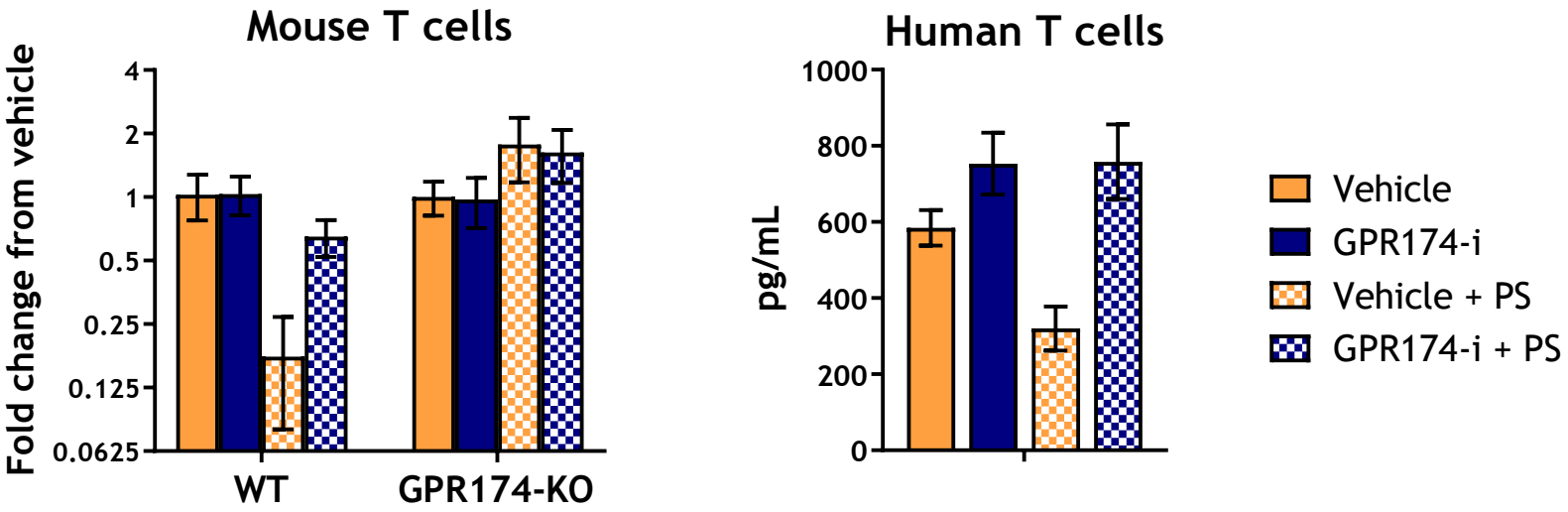
cAMP + cAMP → *Immune suppression*

**GPR174 and A2A/A2B adenosine receptors suppress T and NK cells through the cAMP pathway**

Image: Journal of Cellular Immunotherapy, 2:2, 2016.

# PS Activity on Purified T Cells Is GPR174-Dependent and Is Inhibited by GPR174-i

## IL-2



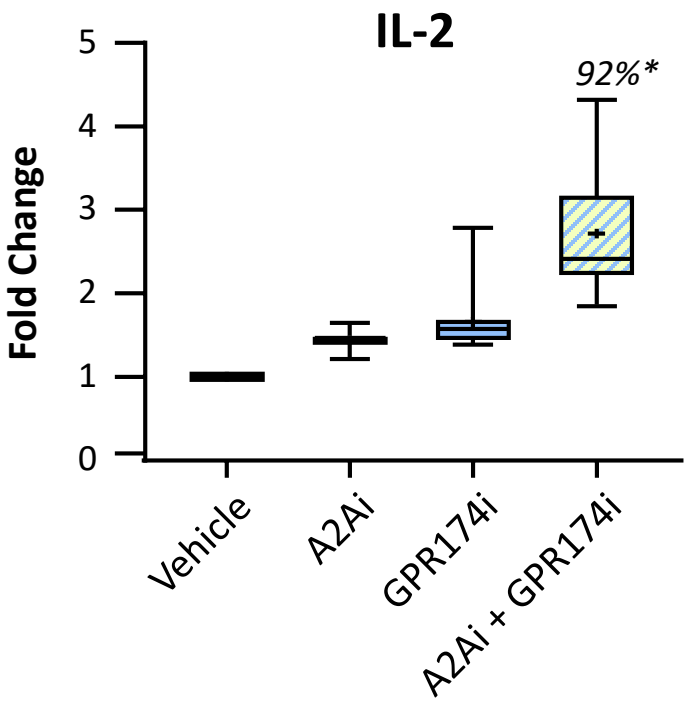

- IFN-γ and TNF are also induced
- Tumor-promoting immune regulators are decreased: CTLA-4, Amphiregulin

# Inhibition of GPR174 and A2A Receptors Synergistically Activates Human T Cells

OMEROS

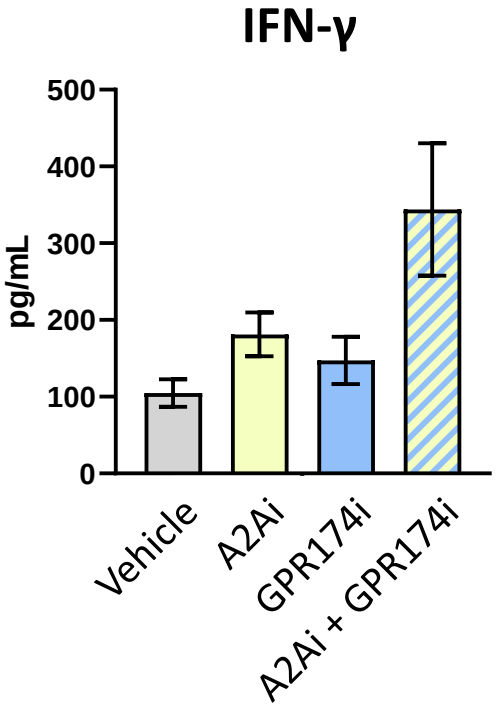
## Total PBMC culture

High cell density, rich in PS and adenosine




## CD8 T cell culture

Low cell density, with supplemented PS and adenosine (NECA)

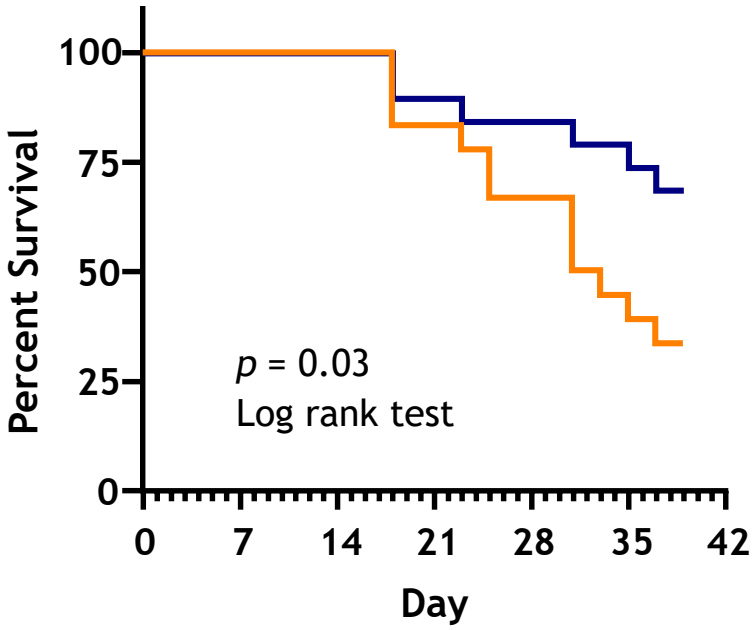



Normalized Data from 12 Human Donors

**Percent of donors exhibiting GPR174i/A2Ai synergy*

# GPR174 Deficiency Activates Anti-Tumor Immunity

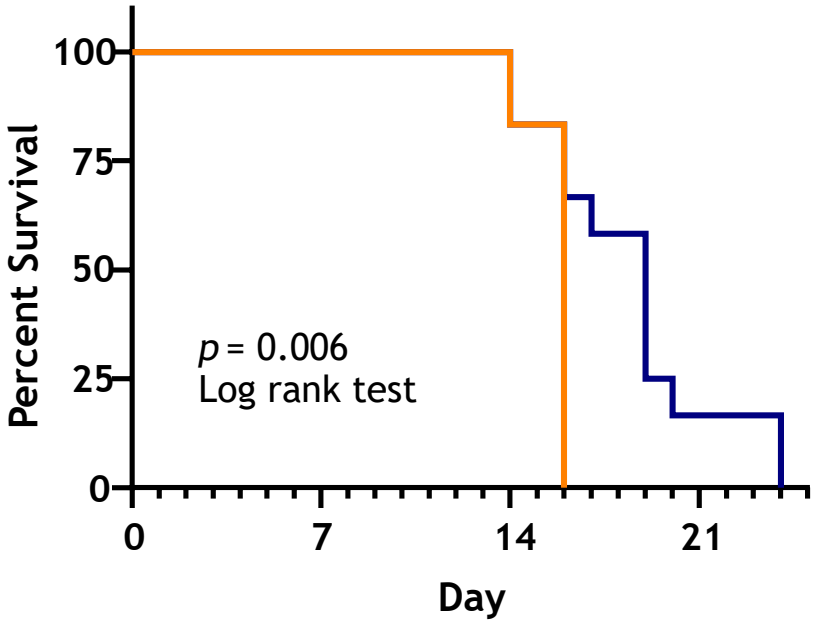
## Colon Carcinoma




WT

KO

## Melanoma




*Anti-GITR co-therapy was used to attenuate Treg dominance in these models

# Next-Generation Therapeutics Transforming Patient Care Today