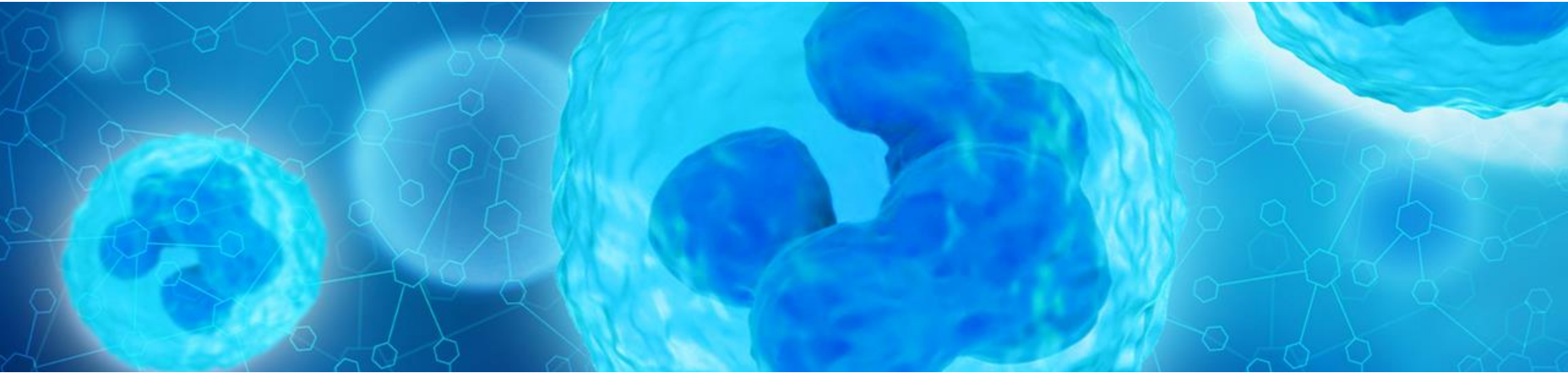
MetrioPharm

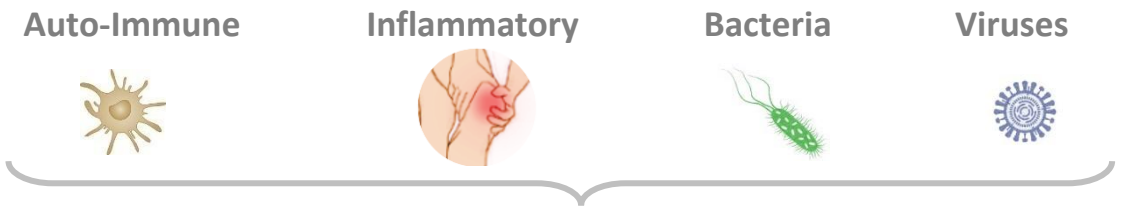
High Tech Innovation Days 2024
September 17-18, 2024, Paris, France

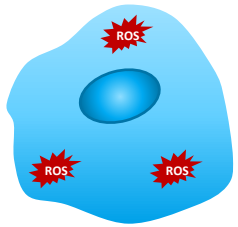


Platform of Immunomodulators Targeting the Mitochondrial Metabolism in Macrophages for Treatment of Inflammatory & Infectious Diseases

MP1032 Modulates the Mitochondrial Energy Metabolism of Macrophages By a First-in-Class Self-regulating Drug Mechanism

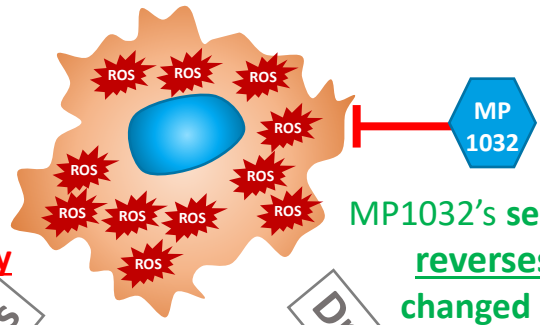
Disturbance of cell energy metabolism (=re-programming) is triggered by…





Macrophage with normal mitochondrial redox balance

Many diseases and pathogens **disrupt (re-programme) cellular/ mitochondrial energy metabolism** with significant downstream effects on driving disease pathology

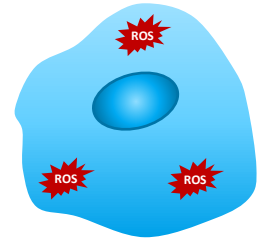


Drives

Macrophage with pathologically changed mitochondrial redox balance

Drives

MP1032's **self-regulated mechanism reverses the pathologically changed mitochondrial redox balance** back to normal



Macrophage with a normalized mitochondrial redox balance

Inflammatory Diseases

Large Indications

Psoriasis | Multiple Sclerosis | Crohn's U. Colitis | Rheumatic Diseases

Orphan

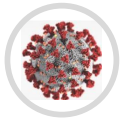
Duchenne Muscular Dystrophy | Juvenile Idiopathic Arthritis

Infectious Diseases

Bacterial

Sepsis Anti-microbial Resistance

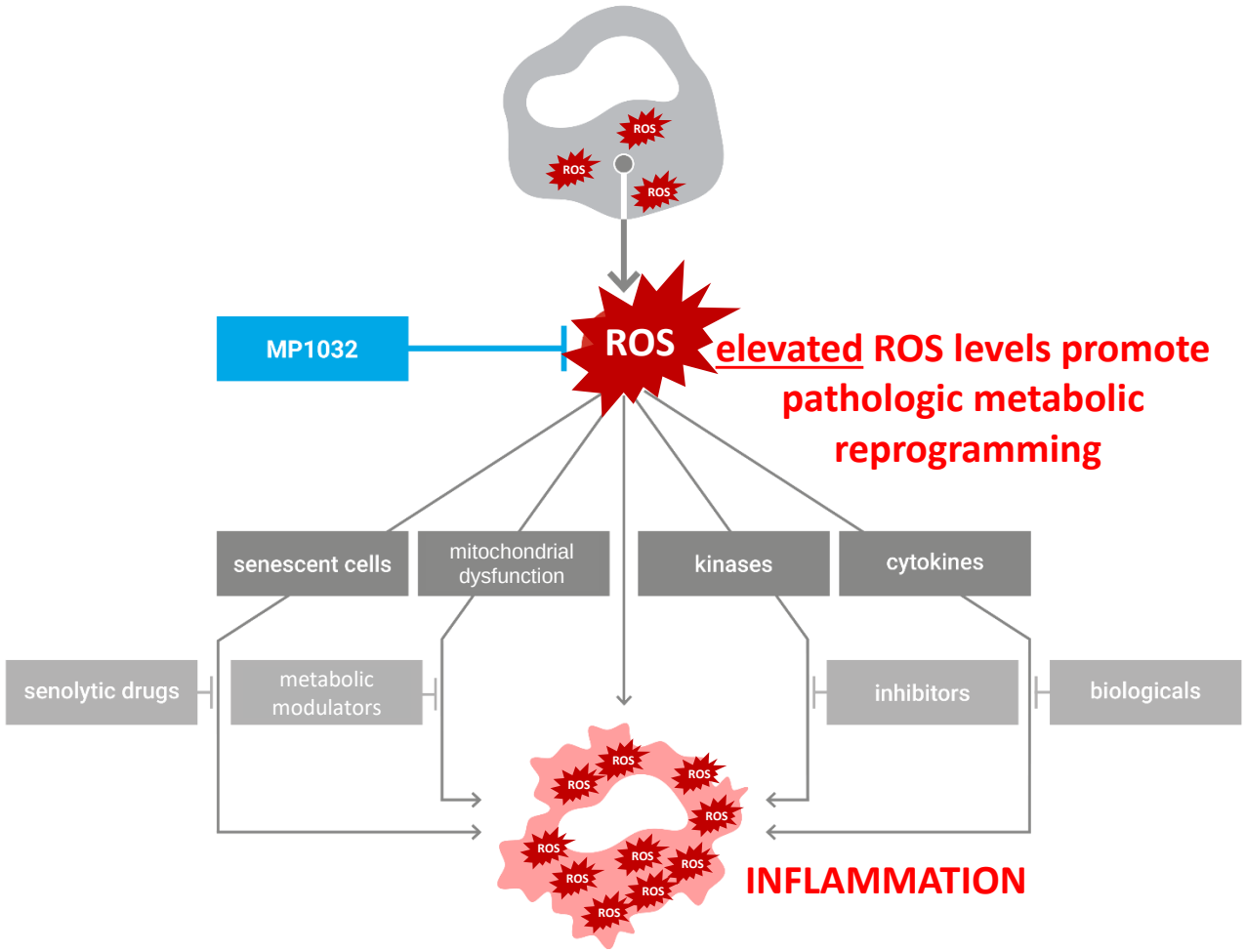
Viral



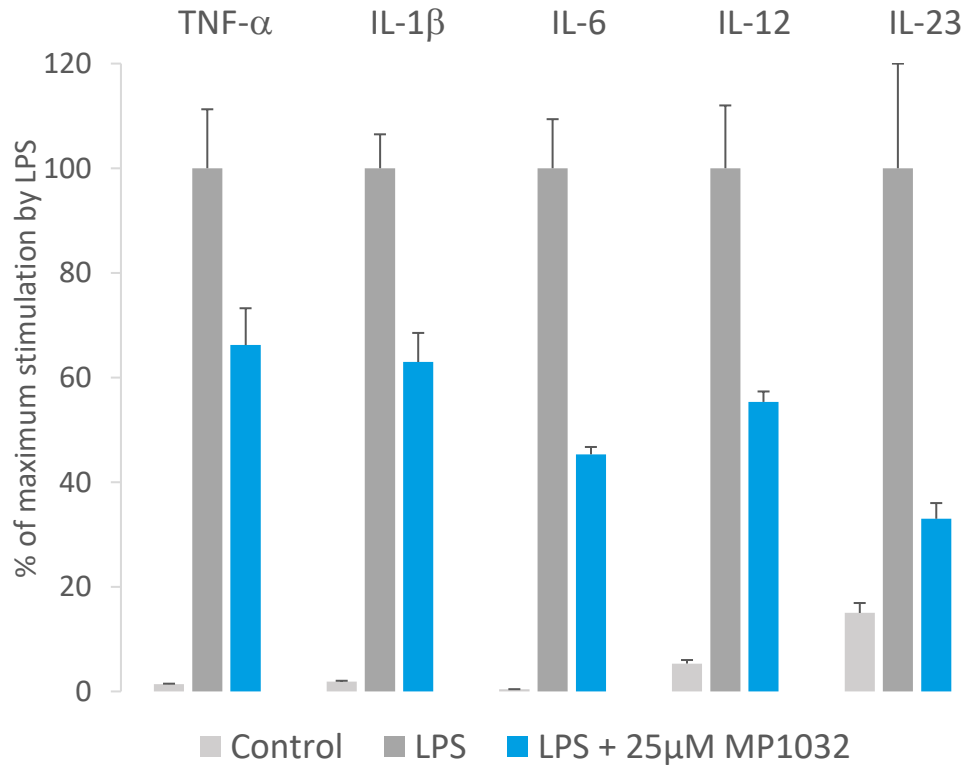
SARS (e.g. SARS-CoV-2) Influenza, RSV

The redox balance of (immune) cells is a key signaling pathway which affects energy metabolism, inflammatory pathways (NFkB, Nrf2), pathogen defense mechanisms and tumor microenvironment. Redox balance is disturbed by metabolic re-programming, which in turn drives disease pathology. MP1032 is a small-molecule metabolic modulator which re-balances cellular redox state.

MP1032 Acts Upstream of Multiple Inflammatory Pathways
Thereby Enhancing the Efficacy of Other Anti-Inflammatory Therapeutics



MP1032 down-modulates major inflammatory cytokines to physiological levels*



* in primary mouse macrophages
LPS: lipopolysaccharides

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First-In-Class Self-Regulated Molecular Mechanism of Action

MP1032 is only Activated by Elevated ROS Concentrations in Immune Cells

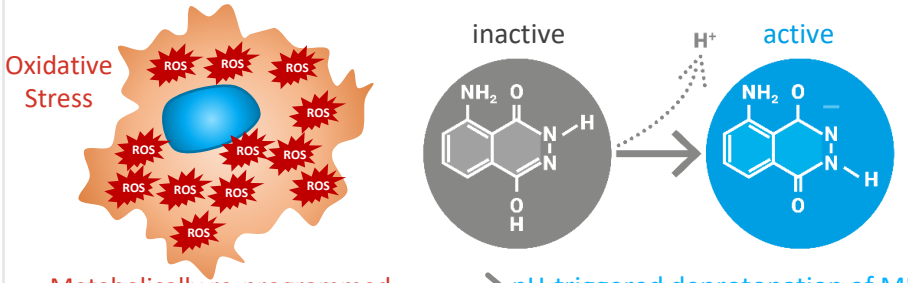
1| Physiologic State

MP1032 remains inactive at physiologic (balanced) redox state

Macrophage with physiologic mitochondrial redox balance → MP1032 **inactive**

2| Pathogenic (Re-Programmed) State

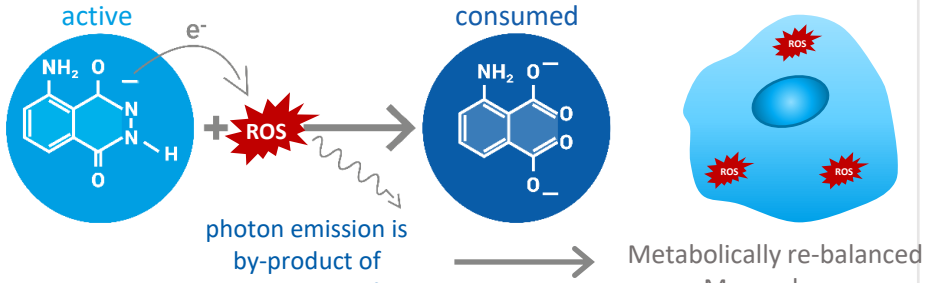
High ROS concentrations create spots of high pH, which **activates** MP1032



Metabolically re-programmed Macrophage → pH-triggered deprotonation of MP1032

3| Balancing Redox State by Electron Transfer

MP1032 modulates cellular redox state by triggered electron transfer

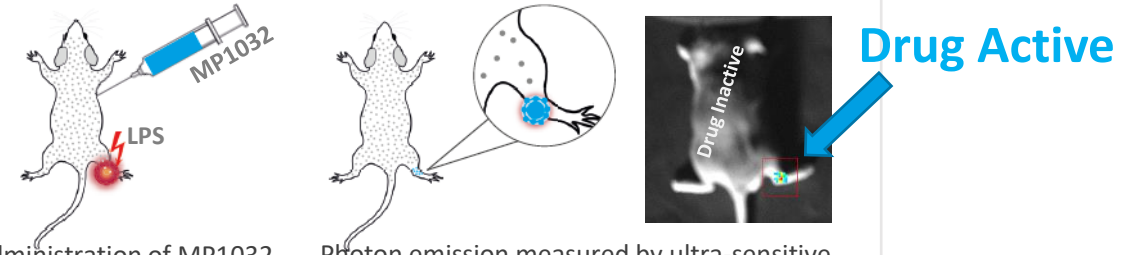


photon emission is by-product of electron transfer

Metabolically re-balanced Macrophage

4| **Targeted** Drug Activity

MP1032 in vivo detection of drug-activity-related photon emission



Systemic administration of MP1032 to animal with LPS-induced localized inflammation

Photon emission measured by ultra-sensitive photon-counting cameras shows **targeted** drug activity only in the affected joint

Due to its molecular structure, MP1032 is **only activated by elevated ROS levels (=oxidative stress) in pathologically metabolically reprogrammed cells.** MP1032 **does not interfere with the normal redox balance that is essential for physiological cell signaling and cell metabolism**. This **self-regulated activation mechanism limits** the redox modulatory effect of MP1032 **exclusively to (immune) cells under oxidative stress**. Once the cellular redox balance is restored, the **activation of additional drug molecules stops** and the **drug activity ceases**. This auto-regulatory activation mechanism ensures that the **modulatory activity of the drug stops** when physiological redox balance is achieved, **without overshooting into reductive stress**.

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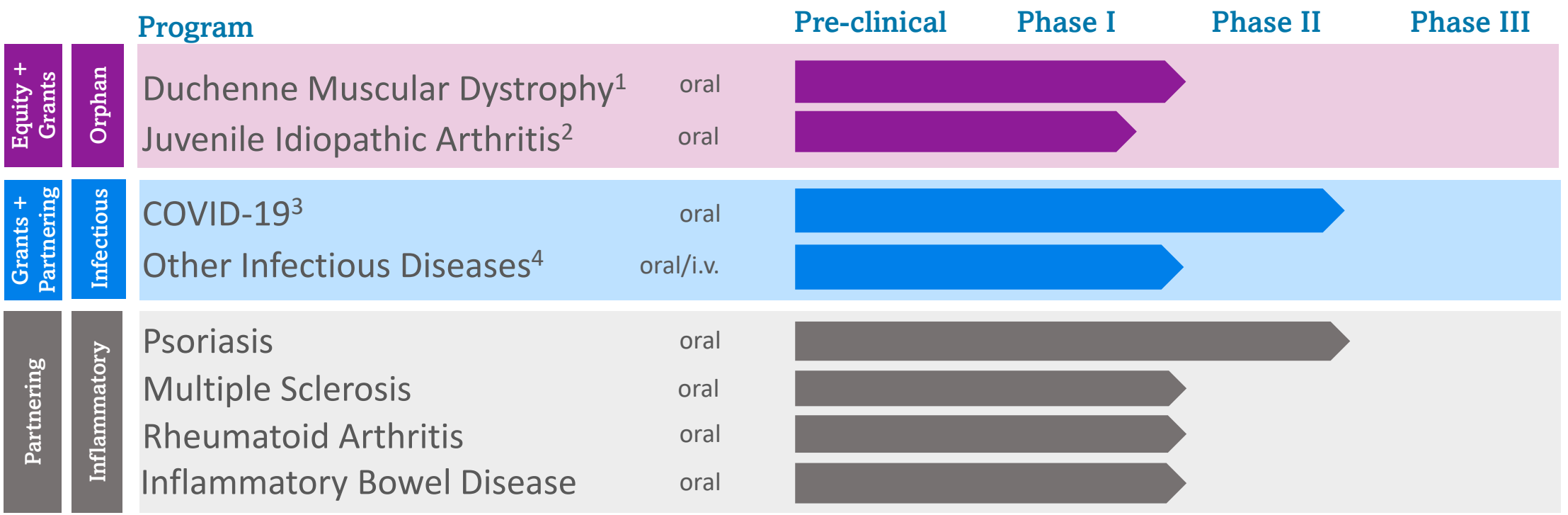
MP1032 Pipeline – Initial Focus on Orphan Diseases



[1] Recently received **Orphan Drug Designation** and **Rare Pediatric Disease Designation from FDA** in 2023; further orphan muscular dystrophy indications such as e.g. **Becker's Muscular Dystrophy** with similar standard anti-inflammatory therapy

[2] On the basis of preclinical in vivo studies for Rheumatoid Arthritis

[3] Phase IIa financed by **EU grant of EUR7.9m**; data were published in ***Lancet Regional Health (Europe);*** this study could serve as PoC for **Host-Directed** Therapies for potentially pandemic infectious diseases such as **COVID, RSV, Influenza** ("**Pandemic Preparedness**")

[4] E.g. **Sepsis,** Multi Drug Resistant Infections, *Clostridioides difficile*, Acute Respiratory Distress Syndrome (ARDS)

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Corporate Strategy 2024-2028

I. Focus on orphan indication(s)

Duchenne muscular dystrophy (replace anti-inflammatory standard therapy of high-dose corticosteroids causing severe side effects)

- Recently received the **Orphan Drug Designation** and **the Rare Pediatric Disease Designation for DMD by the US FDA (Pediatric Voucher** valued and paid for by large pharmaceutical companies **in excess of USD 100 million**)
- **Accelerate regulatory** path by **PRIME** and **Break-Through Designations** in the EU & US
- Support from **international KOLs & various patient advocacy groups (PPMD, Duchenne UK and others)**
- Conduct **Phase IIa & IIb in Europe and the US** and apply for **conditional/accelerated approvals at start of Phase III**
- Participate in **early access programs**, such as the ATU program in France or similar programs in UK and Italy
- Reach important value inflection point after **phase II**: **Conditional Marketing Authorization** (EMA) / **Accelerated Approval** (US-FDA)

II. Raise at least CHF 20 M (up to CHF 40M) equity financing

- Thereof recently raised **CHF 18 M -> 2nd closing in 2024/2025**

III. Further financing by grants (public & from charities) and/or by pharma partnering for

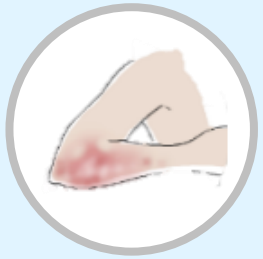
- Clinical trials for **Duchenne Muscular Dystrophy** (DMD) and **other orphan indications** in US & Europe
- **COVID-19** as proof of concept for **host-directed therapy (HDT)** for **(potentially pandemic) infectious diseases**

IV. Partnering (preferably in China, Japan & Korea)

- Find partner for **DMD, (Long) COVID, Psoriasis, Multiple Sclerosis, Rheumatoid Arthritis, Inflammatory Bowel Disease, Sepsis**
- **Conduct phase IIa studies to be financed by partner(s) and/or grants**

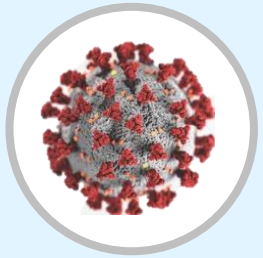
Proven Efficacy and Safety

Efficacy and safety studies conducted with MP1032 as stand-alone drug (monotherapy)



Efficacy ✓
Safety ✓

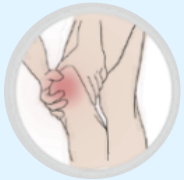
Psoriasis



Efficacy ✓
Safety ✓

COVID-19

- Outstanding safety demonstrated in over 234 patients treated with MP1032 in 4 double-blind placebo-controlled clinical trials.
- Anti-inflammatory and disease-modifying effect demonstrated in two Phase II trials in psoriasis.
- Anti-inflammatory and anti-infective effect shown in a recent Phase II study in COVID-19 patients



Rheumatic Diseases

Crohn's U. Colitis

Multiple Sclerosis

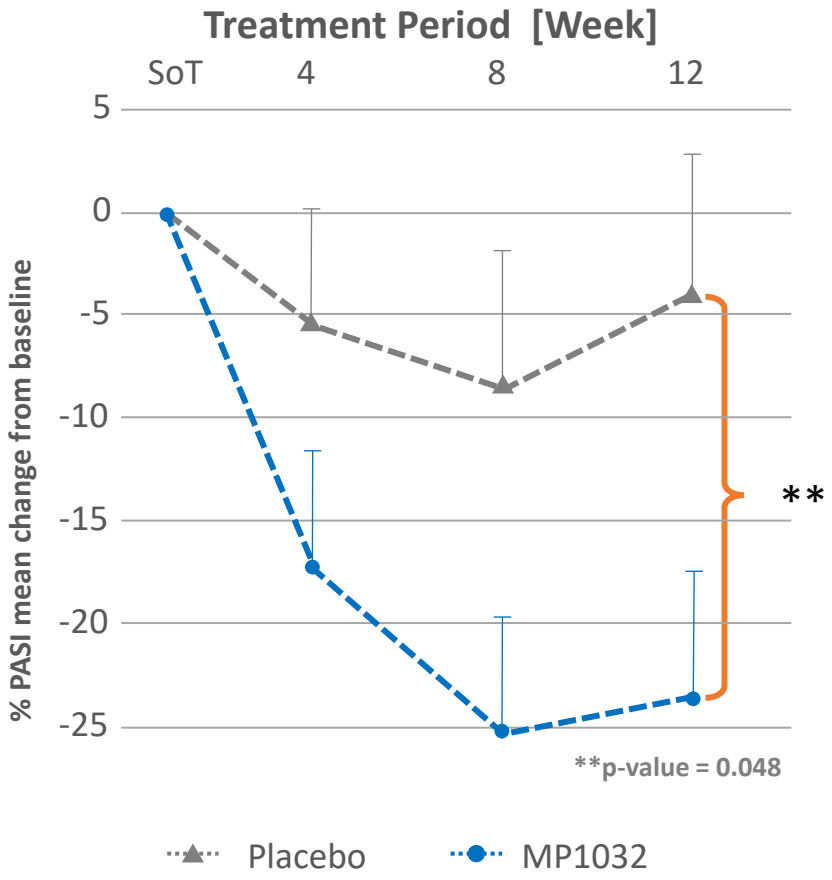
Duchenne Muscular Dystrophy

- Efficacy and therapeutic effectiveness demonstrated in pre-clinical (animal) models of common chronic inflammatory diseases and in animal model of the orphan childhood disease Duchenne Muscular Dystrophy.

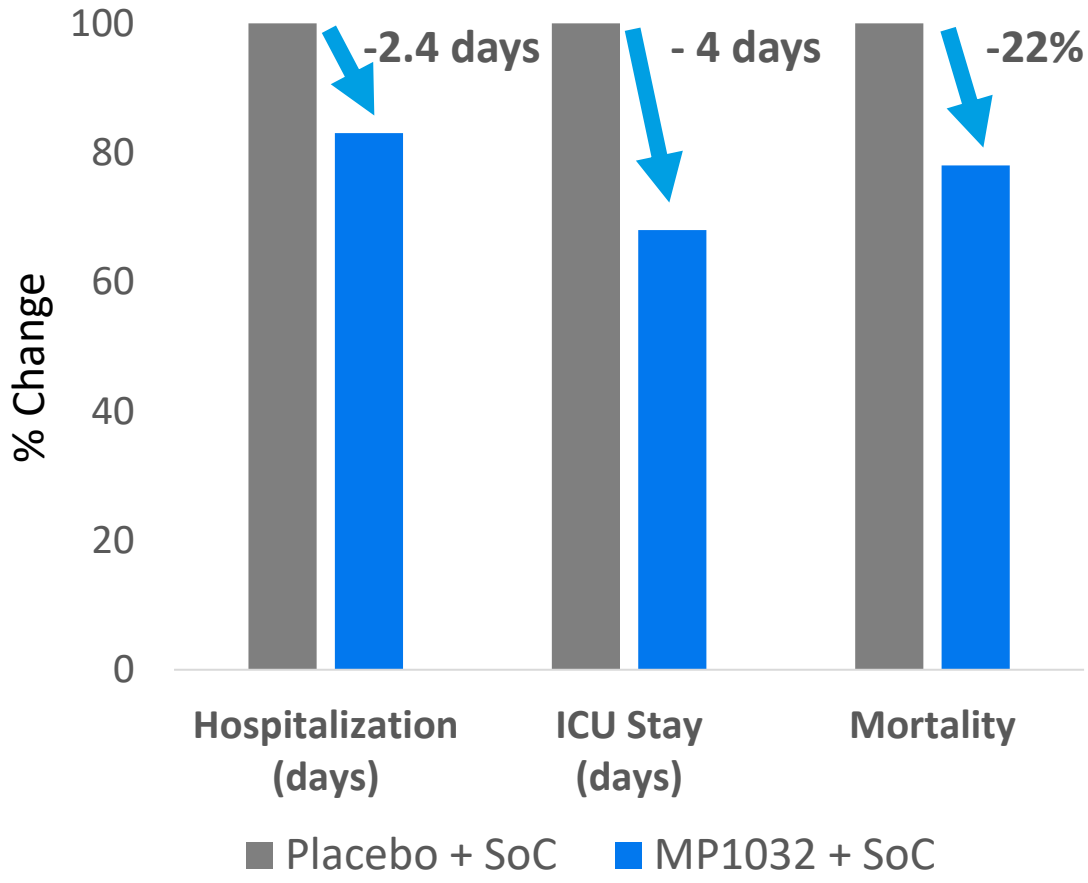
Clinical Data

3 Completed Phase II PoC Studies Demonstrated Disease-Modifying Efficacy and Outstanding Safety

Plaque Psoriasis (PASI 10-15) Phase IIa



Moderate-to-Severe COVID-19 Phase IIa*



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*Data were published in February 2024 in **Lancet Regional Health - Europe**

MP1032 Safety

Outstanding Safety Profile Pre-Clinically and in Humans

Pre-clinical

Max. oral dosing
6 months –
120x human dose
No dose-limiting toxicity could be reached

Max. oral dosing
12 months
30 x human dose
No observed adverse effect

Clinical

Phase 1
Max. oral repeat dose
600 mg
No safety issues detected

Phase 2a
Psoriasis
Max. oral repeat dose
200 mg
No safety issues detected

Phase 2
Psoriasis
Max. oral repeat dose
600 mg
No safety issues detected

Phase 2a
COVID-19
Max. oral repeat dose
600 mg
No safety issues detected

Oral MP1032

MP1032 demonstrated excellent safety based on data from preclinical studies and four clinical trials with 366 patients (= **234 verum** + 132 placebo).

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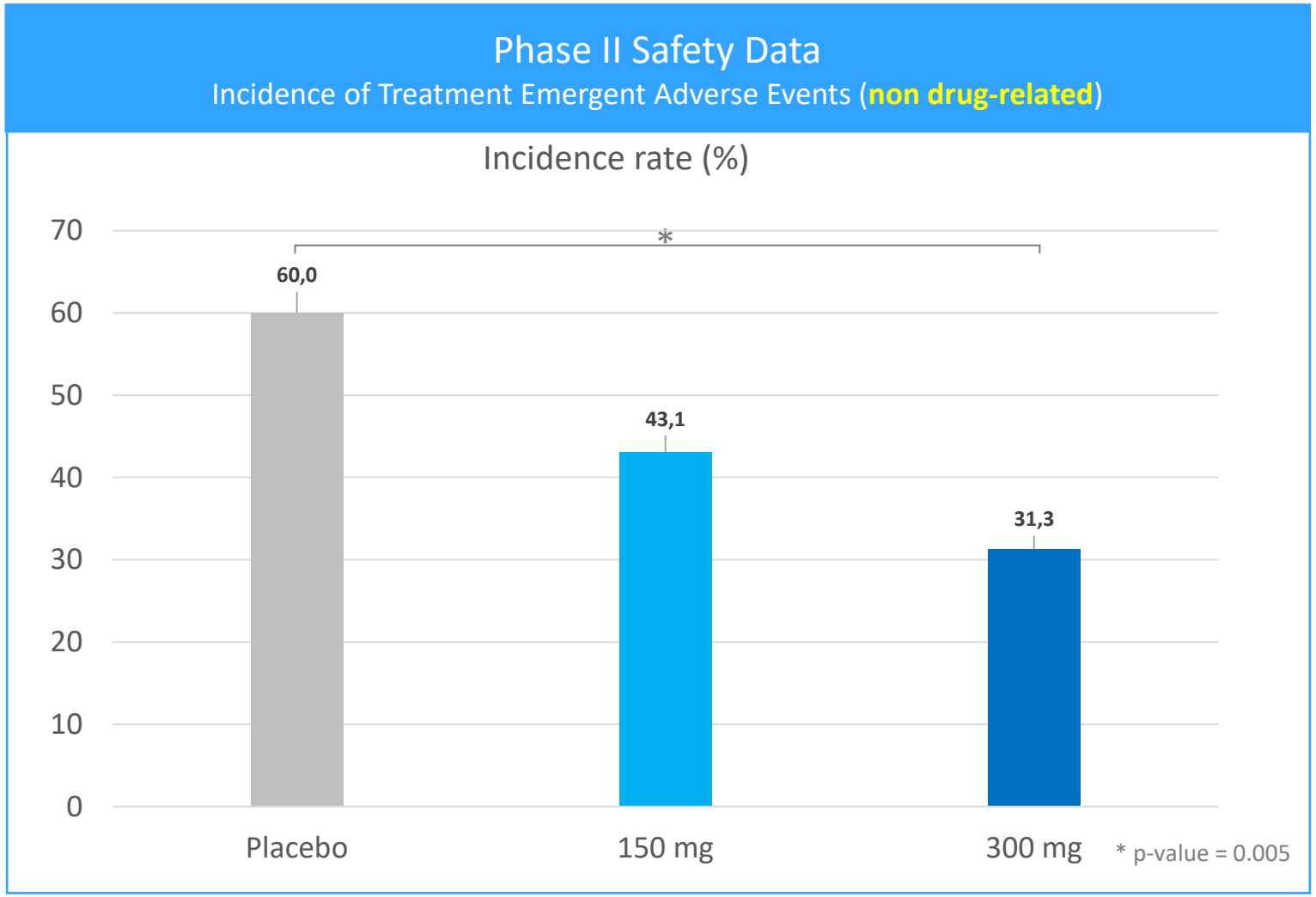
MP1032: Less TEAEs in Treatment Groups than in Placebo Group

Potential to Reduce Non-Drug-Related Adverse-Events in Fixed-Dose Combinations (FDCs)



Safety data from Phase II clinical trial MP1032-CT04 Plaque Psoriasis

155 patients; 3 months daily oral

55 placebo b.i.d.
52 150 mg b.i.d.
48 300 mg b.i.d.

No SAE in MP1032 Groups

150mg and 300 mg doses *reduce* TEAEs

SAE = Serious Adverse Event

TEAE = Treatment Emergent Adverse Events

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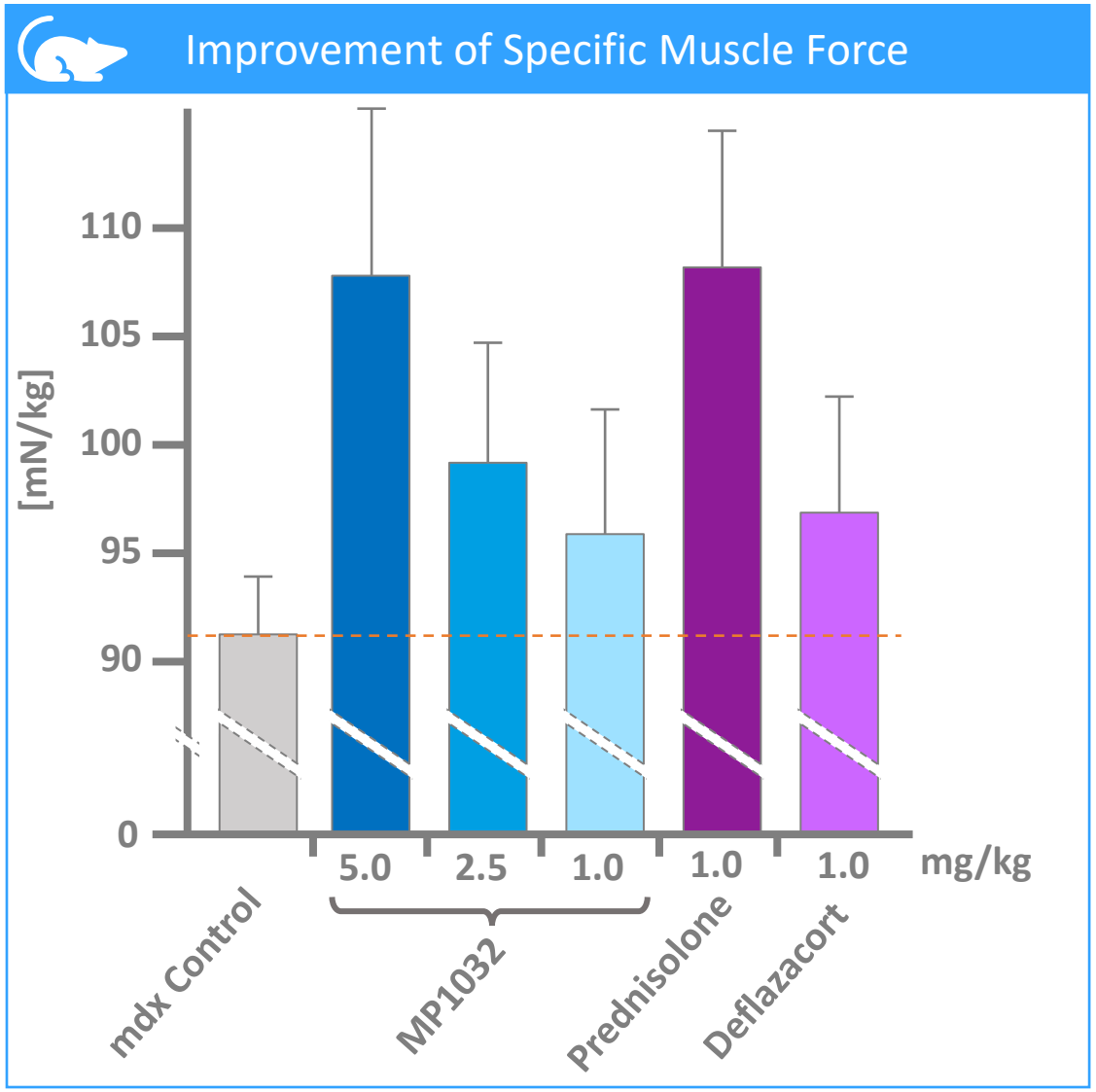
MP1032 Muscle Force Preservation Equal or Better Than Corticosteroids

in DMD Animal Model (mdx mice)



MP1032 improves EDL* muscle force from DMD *mdx* mice with same potency as corticosteroids…

(without any side effects as demonstrated in clinical phase I and II studies)

* EDL = extensor digitorum longus

Study performed by Agada Research Ltd. Halifax, Canada

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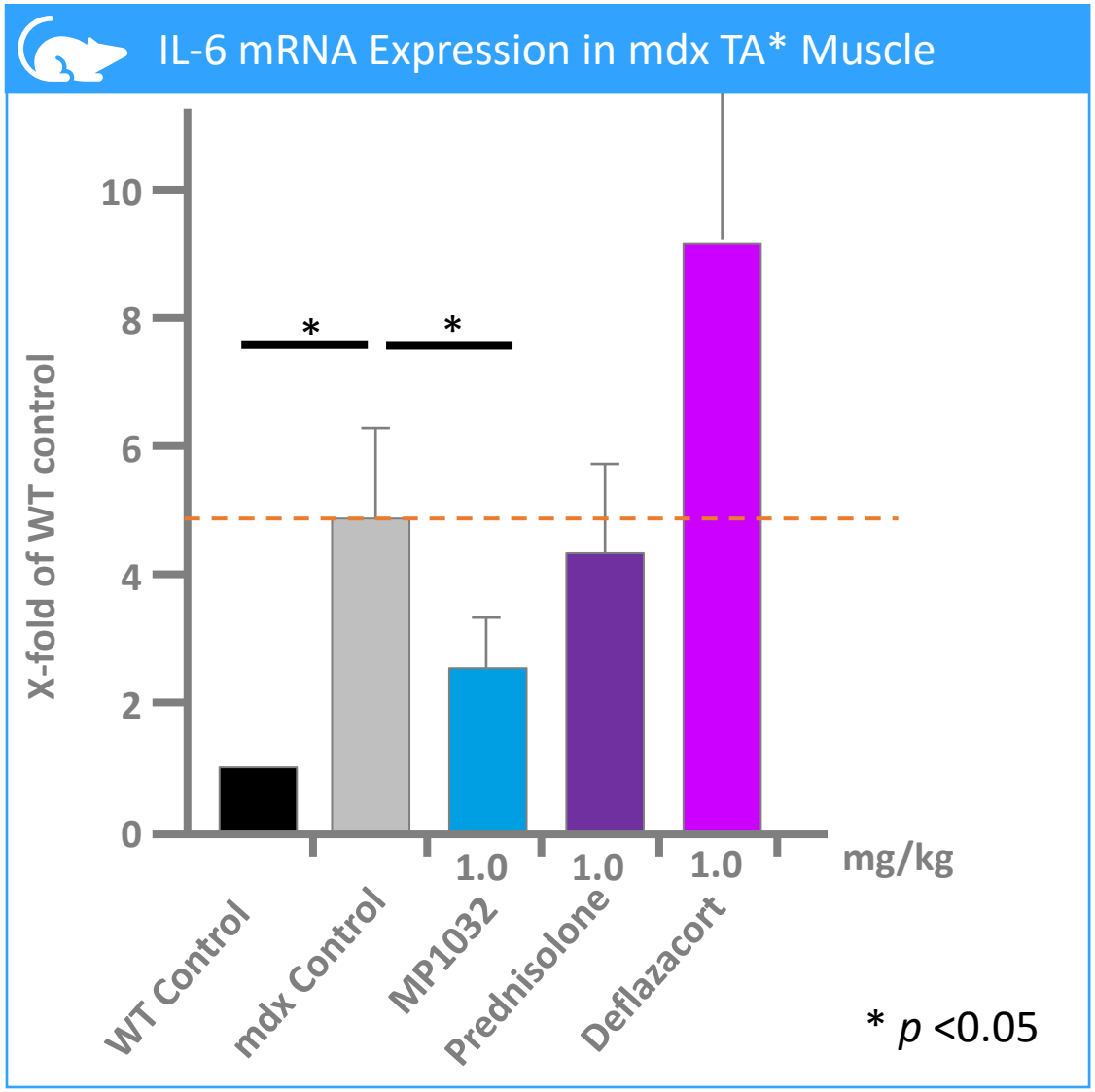
MP1032 – IL-6 Inhibition in Muscle by MP1032 is Better than by Corticosteroids

in DMD Animal Model (mdx mice)



MP1032 elicits meaningful inhibition of IL-6 in TA* muscle of *mdx* mice.

This cytokine inhibitory effect was also seen for IL-1β, TNF-α and CD163 and underlines the efficacy of MP1032 in treatment of DMD.

* TA = Tibialis Anterior

Study performed by Agada Research Ltd. Halifax, Canada

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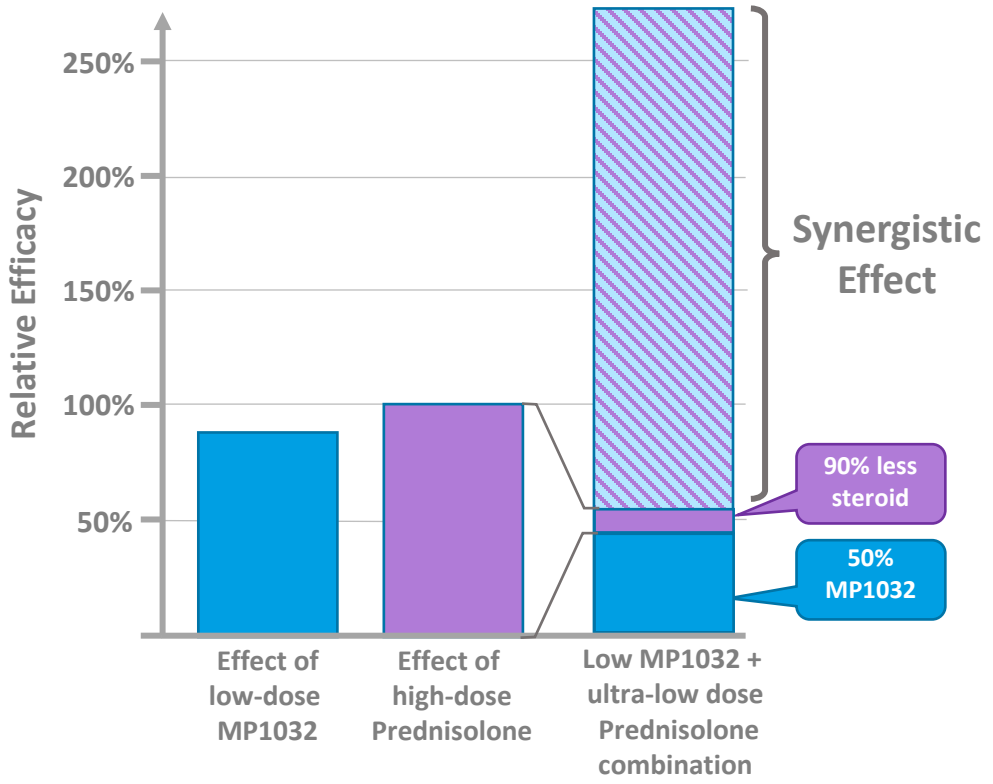
MP1032 Boosts Corticosteroid Anti-Inflammatory Potency

Efficacy ⇈ Side-effects ⇊

Cumulative Synergistic Effect on Cytokine Panel



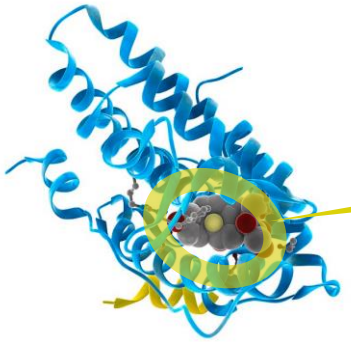
BioMap Assay performed by Eurofins

Oncology

Oncology 2000;59(suppl 1):13–18

Redox Regulation of the Nuclear Receptor

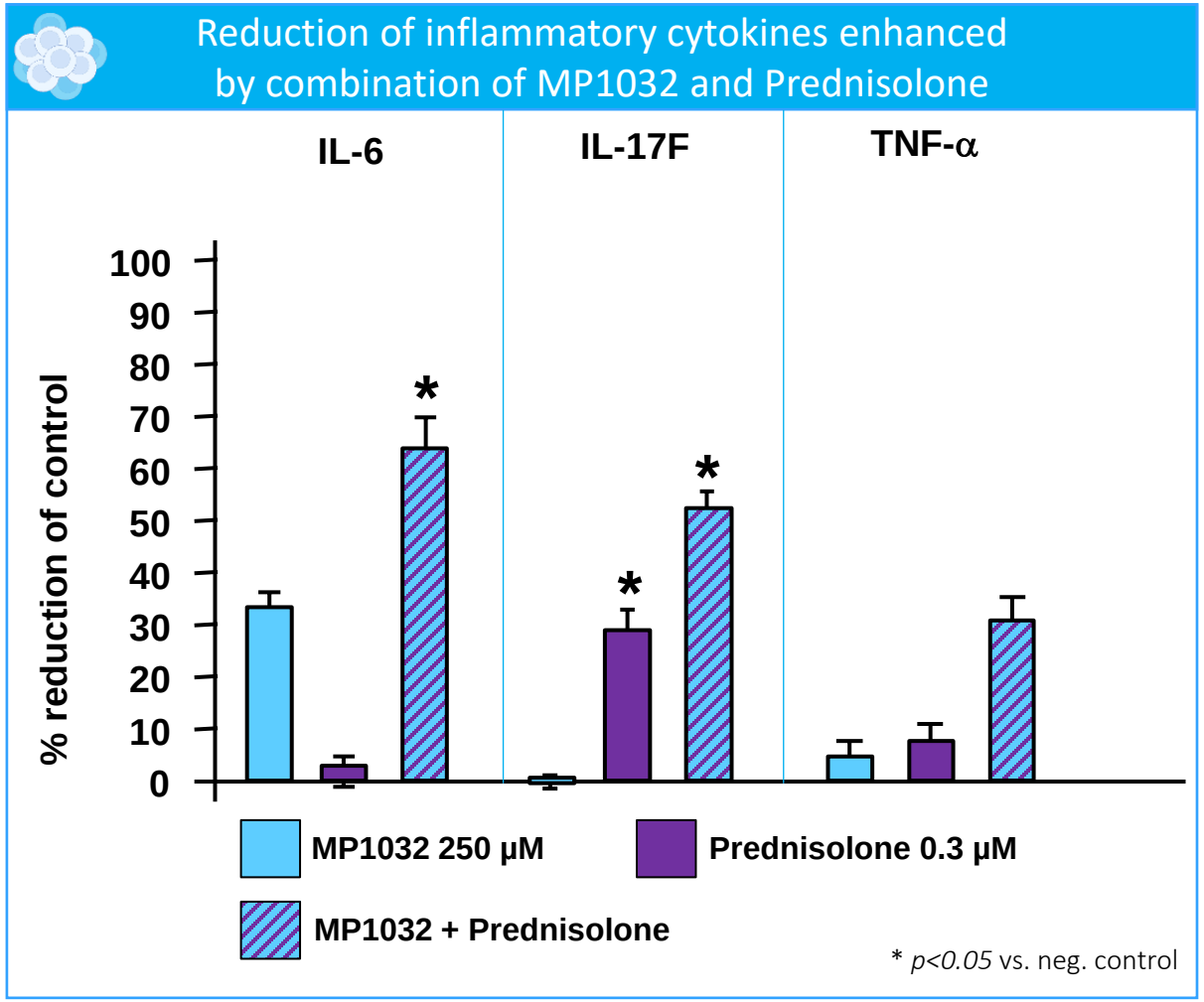
Hirotoshi Tanaka[a] Yuichi Makino[b] Kensaku Okamoto[b] Takahisa Iida[b] Noritada Yoshikawa[b] Takanori Miura[b]



Redox-sensitive region (Cys 481) in vicinity of GCR Ligand Binding Domain

The **synergistic effect** is probably due to the **glucocorticoid receptor's cysteine-rich ligand binding domain**, which is **sensitive to changes caused by redox changes**/oxidative stress/ROS. This weakens steroid binding in cells under oxidative stress, **necessitating higher steroid doses for the same effect. MP1032 can reverse these changes** and **restores optimal steroid binding**. Thus, **MP1032 enables lower doses of glucocorticoids**.

Synergistic Effects of MP1032 in Combination with Prednisolone



Synergistic anti-inflammatory effect of MP1032 with Prednisolone

MP1032 synergistically enhances Prednisolone-induced reduction of inflammatory cytokines IL-6, IL-17F and TNF-α in stimulated human cells.

A similar effect was found with MP1032 and Vamorolone.

This underlines the steroid-sparing effect of MP1032

BioMap BT Cell System Assay performed by Eurofins

MP1032 and DMD: Summary of Experimental Data and Rationale

Experimental data with MP1032

- Reduces pro-inflammatory cytokines like IL-6, IL-1b and TNF-α *(in vitro)*
- Reduces inflammatory foci in muscles of *mdx* mice
- Improves *ex vivo* muscle specific force in *mdx* mice, dose dependent, similar to steroid treatment
- Lacks growth-related side effects of Corticosteroids in mice
- Acts synergistically with Prednisolone and Vamolorone to reduce IL-17a *(in vitro)*

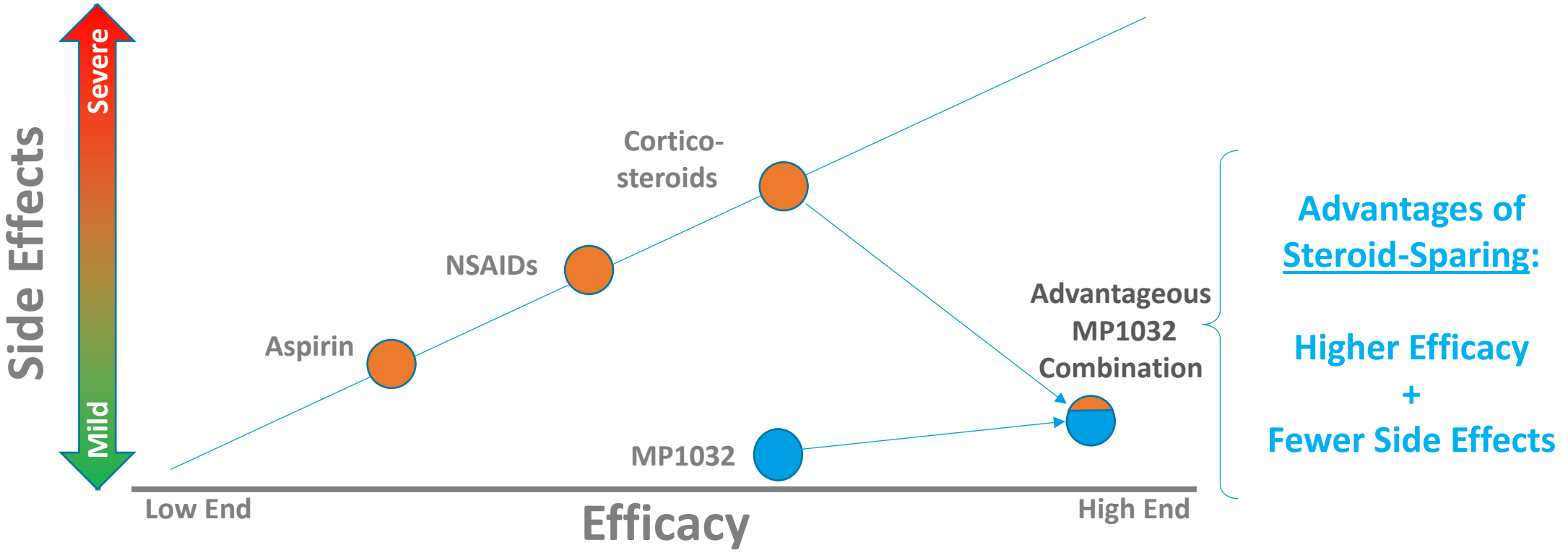
Rationale & Benefits of MP1032 as DMD therapy

- Inflammation in muscles is a major issue in DMD
  - MP1032 is anti-inflammatory
- Current therapies with long-time use of steroids (e.g. Prednisolone or Vamorolone) cause serious side effects
  - MP1032 has nearly no side effects (as demonstrated in Phase I and Phase II studies)
  - MP1032 synergistically enhances effects of Corticosteroids, suggesting a steroid-sparing use
- Other approved therapies e.g. like Ataluren (Translarna®) only suitable for small subset of DMD patients
  - In contrast, MP1032 not restricted to subsets of patients (due to its MoA)

Next Steps

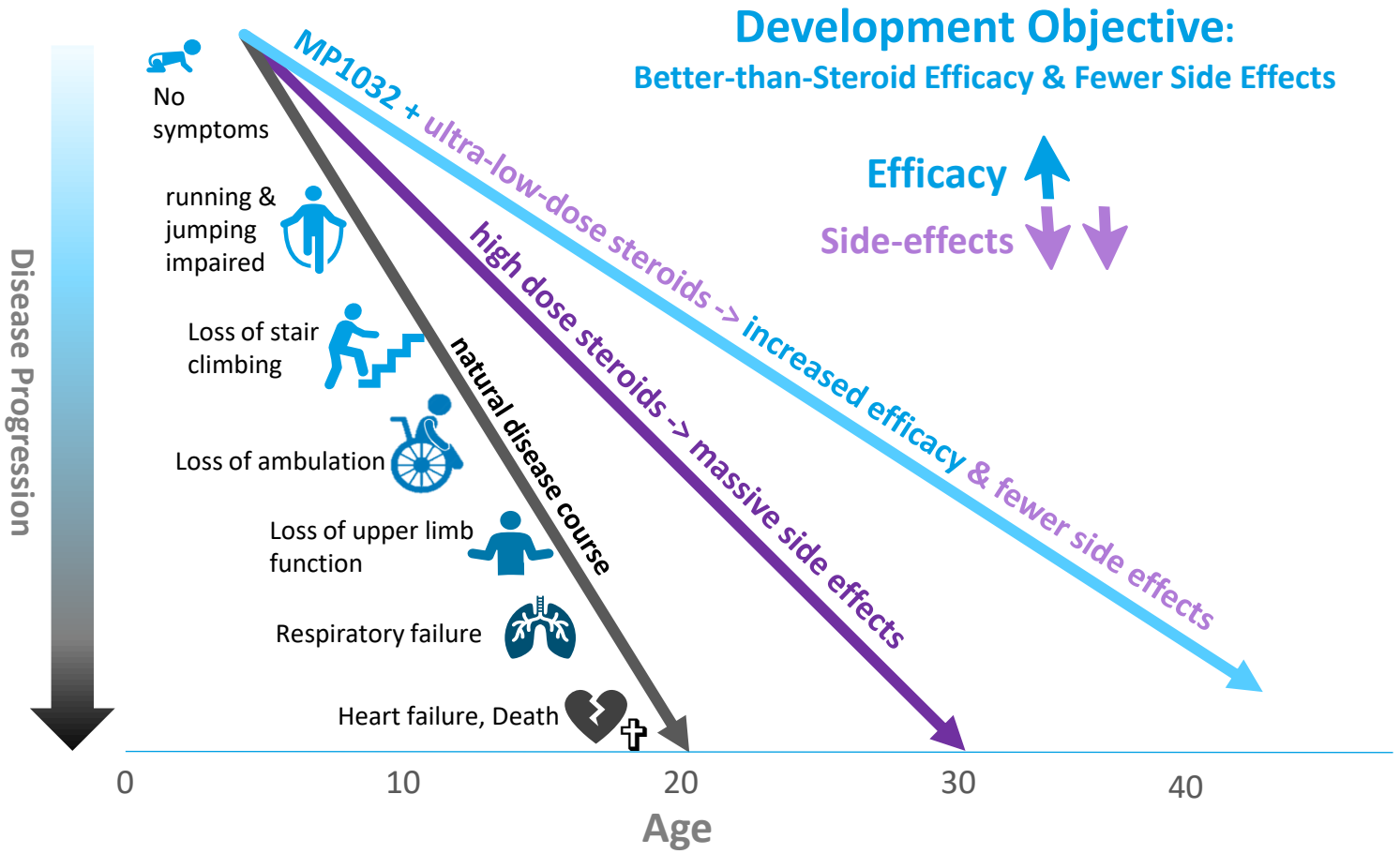
- MetrioPharm plans an open-label Phase IIa clinical study, starting in 2025
- Proposals of CROs are currently investigated

Combinatorial Drug Repositioning Strategy in DMD, Rheumatoid Arthritis & further Indications with Corticosteroid Standard Therapies



Immune Metabolic Modulation (MP1032) **boosts the efficacy** of existing anti-inflammatory drugs like corticosteroids in a **highly supra-additive way**. This allows for the creation of a **new class** of next-generation fixed-dose-combination drugs with **improved efficacies and fewer side effects from corticosteroids in a large range of indications**

Duchenne Muscular Dystrophy (DMD)



Steroid side effects

- Growth retardation
- Cushing syndrome
- Osteoporosis
- Hypertension
- Behavioral changes

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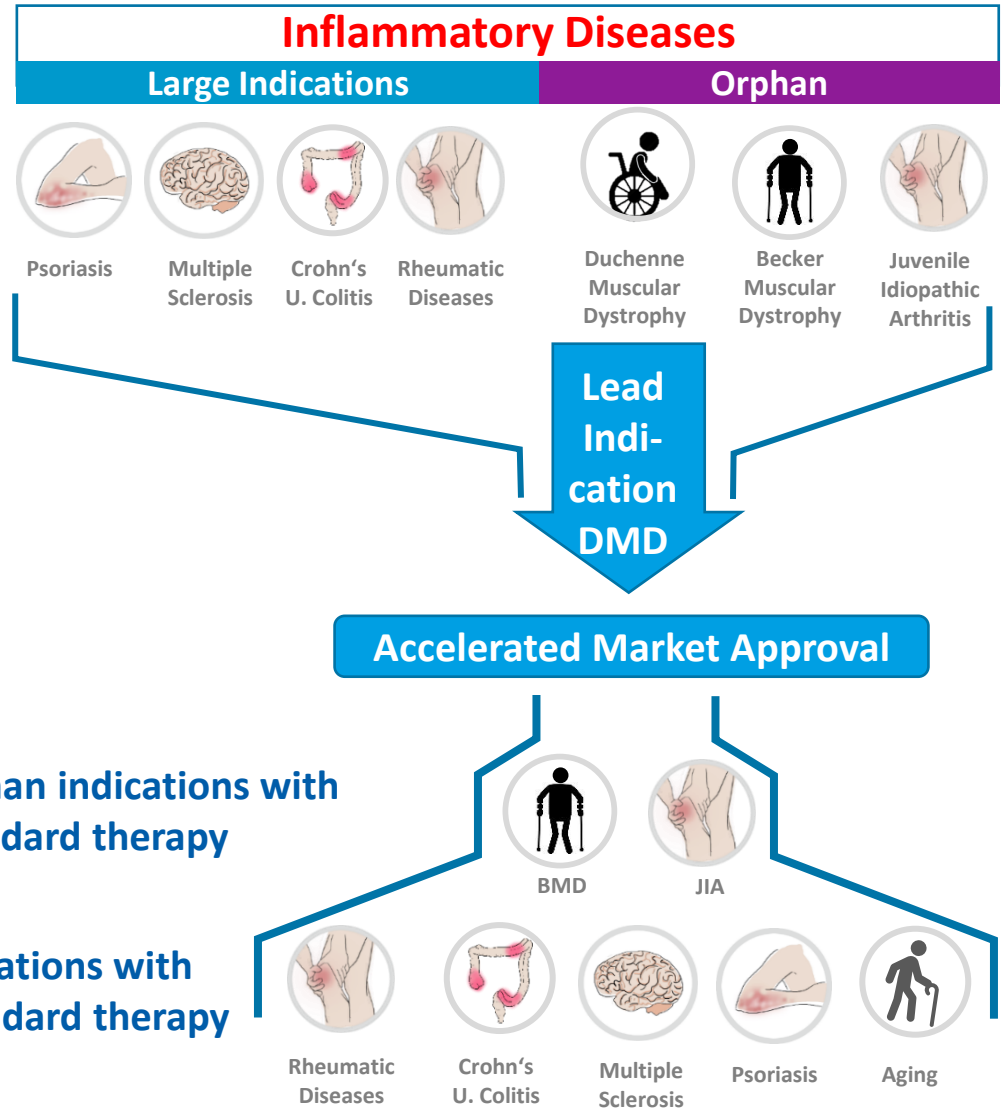
Development Strategy: Initial Focus on Orphan Diseases



Duchenne Muscular Dystrophy

- **High medical need**
- **Orphan disease**
- **Regulatory fast track**
- **Strong support from patient organizations**

Expansion into other orphan indications with similar corticosteroid standard therapy

Expansion into large indications with similar corticosteroid standard therapy

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Corticosteroid Sparing – A Significant Market Opportunity

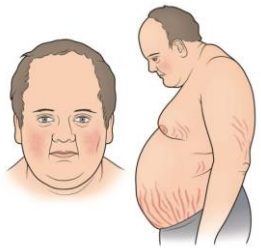
Corticosteroids: still the most widely used therapy for e.g.

Orphan Opportunities	Large Non-orphan Indications		
• **Duchenne Musc. Dystrophy** • Juvenile Idiopathic Arthritis • Becker Muscular Dystrophy • Other Muscular Dystrophys • Autoimmune Hepatitis	• **Psoriasis** • **Rheumatoid Arthritis** • **Inflammatory Bowel Disease** • **Multiple Sclerosis** • **COVID-19 (hospitalized)**	• Syst. Lupus erythematosus • Sarcoidosis • Polymyalgia Rheumatica • Polymyositis • Urticaria	• Asthma • COPD • Interstitial Lung Disease • Rhinitis • Contact Dermatitis

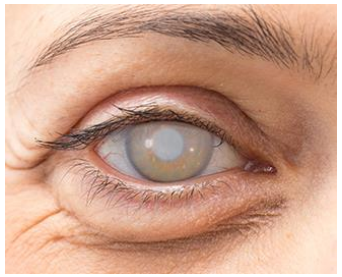
Corticosteroids: highly effective - but problematic side-effect profile

Heart Damage

Osteoporosis



Cushing Syndrome



Eye Damage

Growth Retardation

+ Further Side Effects

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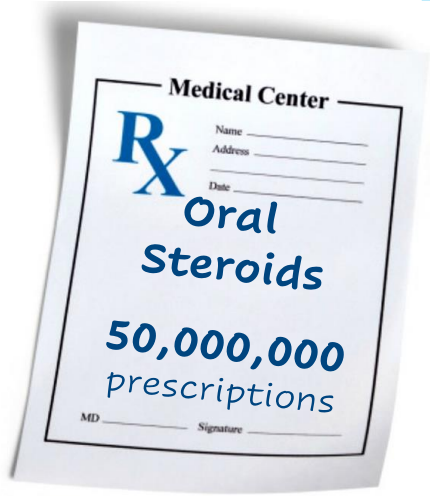
Glucocorticoid Market Opportunity

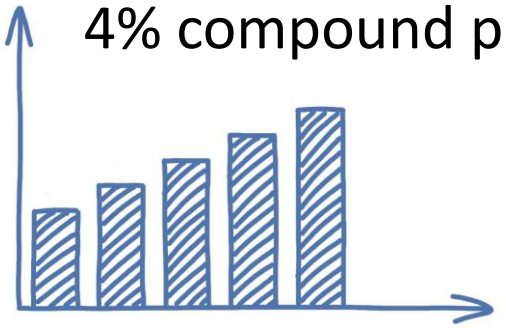


5 Big EU

Total Addressable Market: Worldwide Estimated >>200 Million Prescriptions per Year

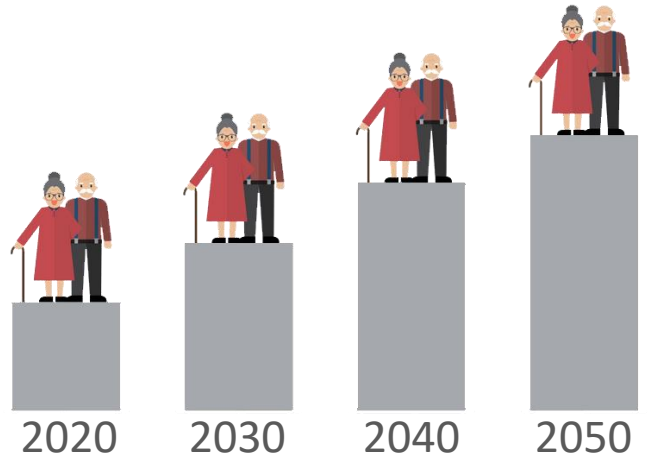
Projected Market Growth

4% compound per year



Growth Drivers:

- Aging
- Demographic Change
- Rise in Chronic Diseases



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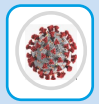
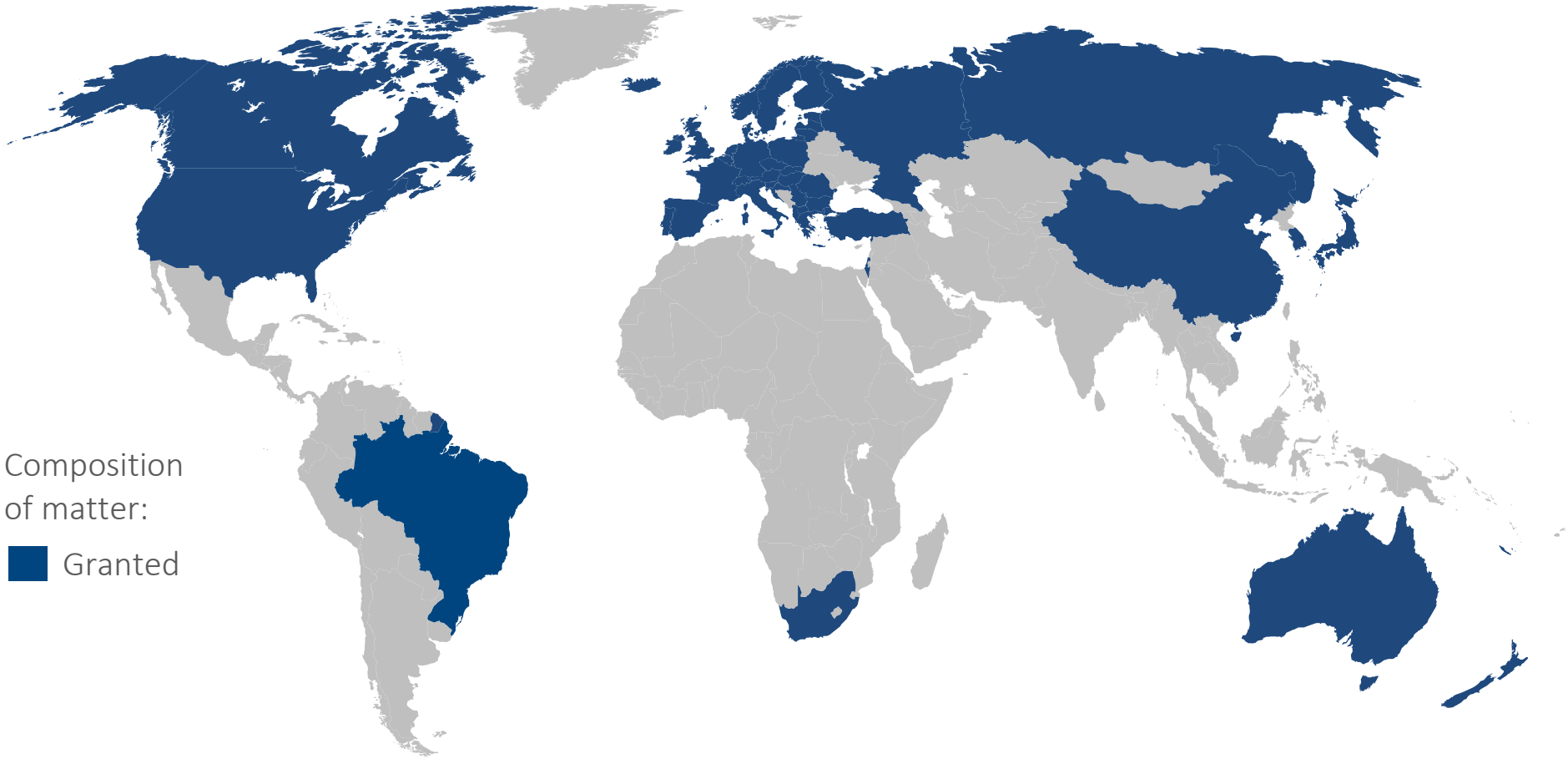
Total Market Size for MetrioPharm Pipeline

Indication	Medical Need & Market Opportunity	Total Market Size
 **Duchenne Muscular Dystrophy**	Steroid-sparing therapies with improved disease-slowing properties and outstanding safety profile (PoC for other inflammatory diseases)	**$ 4 Billion**
 **Juvenile Idiopathic Arthritis**	Steroid-sparing therapies with improved disease-slowing properties and outstanding safety profile (PoC for other inflammatory diseases, see below)	**$ 2 Billion**
 **Psoriasis**	A safer and more effective oral drug, especially for the large, underserved segment of mild-to-moderate psoriasis (e.g. by steroid-sparing)	**$ 26 Billion**
 **Multiple Sclerosis**	A more effective oral therapy with better tolerability compared to currently leading drugs (e.g. by steroid-sparing or other fixed-dose combinations)	**$ 24 Billion**
 **Inflammatory Bowel Disease**	Oral maintenance therapies with higher response rates than salicylates and better long-term safety than corticosteroids (by steroid-sparing)	**$ 20 Billion**
 **Rheumatoid Arthritis**	An effective, oral early-intervention treatment for safe long-term use (e.g. by steroid-sparing)	**$ 28 Billion**
 **COVID-19/Long COVID & other pandemic infectious diseases**	1. **Virus-variant-independent** oral drug for safe **prophylactic & early intervention use** in **immune-compromised patients** & **Long/Post COVID** 2. PoC for host-directed therapies for other (potentially pandemic) infectious diseases such as **Influenza Virus, Respiratory Syncytial Virus** & others (see below)	**$?? Billion**
 **Other Infectious Diseases**	Host-directed therapy for **Sepsis,** Multi Drug Resistant Infections, Clostridioides difficile, Acute Respiratory Distress Syndrome (ARDS) etc.	**$ 10+ Billion**

Strong Intellectual Property Portfolio



- Strong intellectual property portfolio with 21 patent families including 98 granted patents to-date
- Composition of matter patents: valid until 2031 (plus PTE/SPC options)
- Medical use patent applications in various fixed-dose combinations: valid until **2042/2043**

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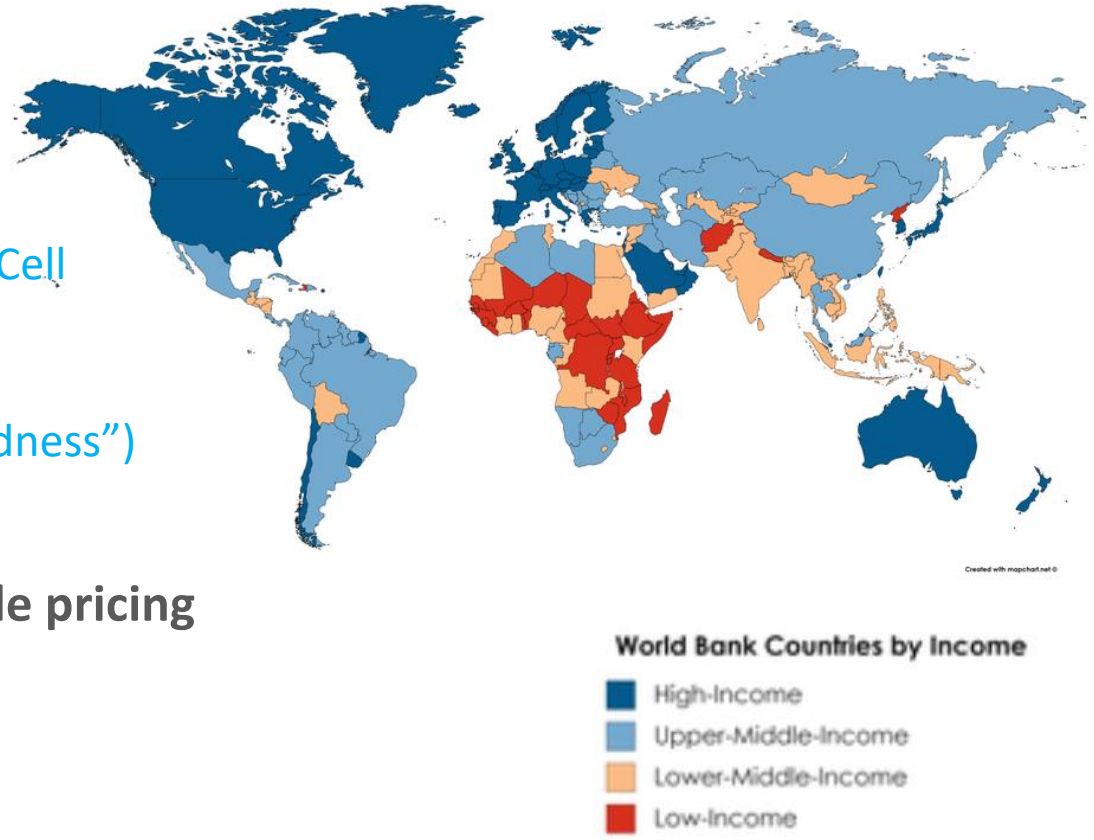
Investment with Social Impact

- **Addresses high medical needs in Low & Middle-Income Countries (L&MICs)**
  - Chronic diseases
    - Affordable alternative to high-end therapies (Biologics, Cell Therapies) which are out of reach for L&MICs
  - Infectious diseases
    - Early response to new viral threats (“Pandemic Preparedness”)
    - Anti-microbial resistance
- **Low Cost-of-Goods (manufacturing) allows for affordable pricing**
- **Ease of use in compromised environments**
  - oral
  - no cooling required
  - highly stable
- **Outstanding safety – no need for expensive patient monitoring**



Experienced Leadership Team

	**Thomas Christély** *Chief Executive Officer*	25+ years of experience in general management, corporate & business development as well as finance at board level of private and public biotech & pharma companies in Europe and the US; developed MYR and sold it to Gilead
	**Wolfgang Brysch MD** *Chief Scientific Officer* *Co-Founder*	25+ years of drug development experience at various biotech companies, co-founder of MetrioPharm and serial entrepreneur; Managing Director of IT-based data management company for R&D; leader of research group at the Max-Planck-Institute, physician
	**Astrid Kaiser PhD** *Head of Drug Development*	20+ years of drug development experience at various biotech companies (Jerini, Mologen); Senior researcher in cancer research at Benjamin Franklin University Hospital, Berlin
	**Ulrich Granzer PhD** *Senior Regulatory Advisor*	Owner and CEO of Granzer Regulatory Consulting (20 y.), worked previously as VP Global Regulatory Affairs at Bayer, VP Global Regulatory Affairs at BASF Pharma; Director Regulatory Affairs at Glaxo
	**Harald Fricke PhD** *Senior Development Advisor*	25+ years of drug development experience at various pharma and biotech companies in Europe and the US – COO & CMO at Apogenix, VP Global Clinical Development at Baxter, Director at GSK
	**Georg Wiebecke PhD** *Senior CMC Advisor*	25+ years of drug manufacturing experience in Europe and the US, Head of CMC Management, Supply Chain and Global Chemical Manufacturing at Roche (17y.), worked previously as strategy consultant at McKinsey (6 y.)

Scientific Advisory Board

Prof Laurent Servais
Professor of Paediatric Neuromuscular Disease, University of Oxford

Laurent Servais, MD, PhD, Professor of Paediatric Neuromuscular Disease at the University of Oxford and invited professor at the University of Liège, specialized in spinal muscular atrophy, Duchenne Muscular Dystrophy, and Myotubular Myopathy. Educated in Medicine, Paediatrics, Child Neurology, and Myology in France and Belgium, he leads two newborn screening programs in UK (SMA) and Belgium (Genomic Newborn screening). His research focuses on innovative outcome measures using wearable devices and newborn screening. He sees patients in UK and in Belgium, and leads annual consultations in Egyptian and Romanian hospitals.

Prof Dirk Fischer
Senior Physician Neuro- and Developmental Pediatrics, University Children's Hospital Basel

Dirk Fischer, MD, PhD, Head of Neuromuscular Research, Senior Consultant of Neuro- and Developmental Pediatrics and Electrophysiology at University Children's Hospital Basel (since 2008). His international studies included stays in Madrid, Dublin, Buenos Aires, and London, as well as a postdoctoral fellowship at the Centre National de la Recherche Scientifique (CNRS) in Paris (2003-2005) focusing on hereditary muscular and peripheral neurological diseases such as Duchenne muscular dystrophy.

Prof Marcus Thelen
Emeritus, Institute for Research in Biomedicine, Bellinzona

Marcus Thelen, PhD, is Honorary Professor at the University of Bern. In 2000, he co-founded the Institute for Research in Biomedicine (IRB) in Bellinzona and headed the Signal Transduction Laboratory until his retirement in 2022. In 1989, he joined the group of Alan Aderem in the Laboratory of Cellular Physiology and Immunology of the Cohn/Steinman Department at Rockefeller University, focusing on cytokine-mediated phagocyte priming and signal transduction. Following a Swiss National Science Foundation award, Marcus led a research group on leukocyte signal transduction in Bern. Marcus received his PhD from the University of Bern, specializing in inflammation and chemokines at the Theodor Kocher Institute.

Prof Ferdinando Nicoletti
Full Professor of General Pathology and Immunology, University of Catania

Ferdinando Nicoletti, MD, PhD, Full Professor of General Pathology and Immunology (since 2011) at the University of Catania (Italy). Graduated at the University of Catania in 1987 in Medicine and Surgery and specialized in Allergology and Clinical Immunology at the University of Milan (Italy) in 1990. Ferdinando Nicoletti has been external consultant at the Institute for Inflammation Research, Righsospitalet University Hospital, Copenhagen, Denmark, from 1999 until 2010; Visiting Professor at the School of Medicine of the University of Belgrade, Serbia, in 2004; Honorary Professor at Tblisi State Medical University (Georgia) in 2023.

Summary (1)
Platform of Oral Modulators Targeting the Mitochondrial Metabolism in Macrophages

- **First-in-class self-regulating modulators of mitochondrial metabolism in macrophages**
  - MP1032 **reverses** the **pathologically altered ("reprogrammed") mitochondrial redox balance in macrophages** back to normal
  - By down-regulating **pathologically elevated levels of ROS** (Reactive Oxygen Species) back to **physiological (normal) levels**
  - **Without (!) interfering with physiological levels of ROS,** which are essential for cell signaling & other functions of all cells
  - Through a **first-in-class self-regulating mechanism of action** that is **activated only** when ROS levels are **elevated (pro-drug)**
  - **Activation** is initiated **through clusters of high pH levels** that trigger **deprotonation** of MP1032 which then degrades ROS
  - Once the cellular **redox balance is restored** to **physiological ROS levels**, the **activation** of further MP1032 molecules **stops**
  - Consequently, the **drug activity ceases**, i.e. MP1032 is completely **inactive at physiological (normal) ROS levels**

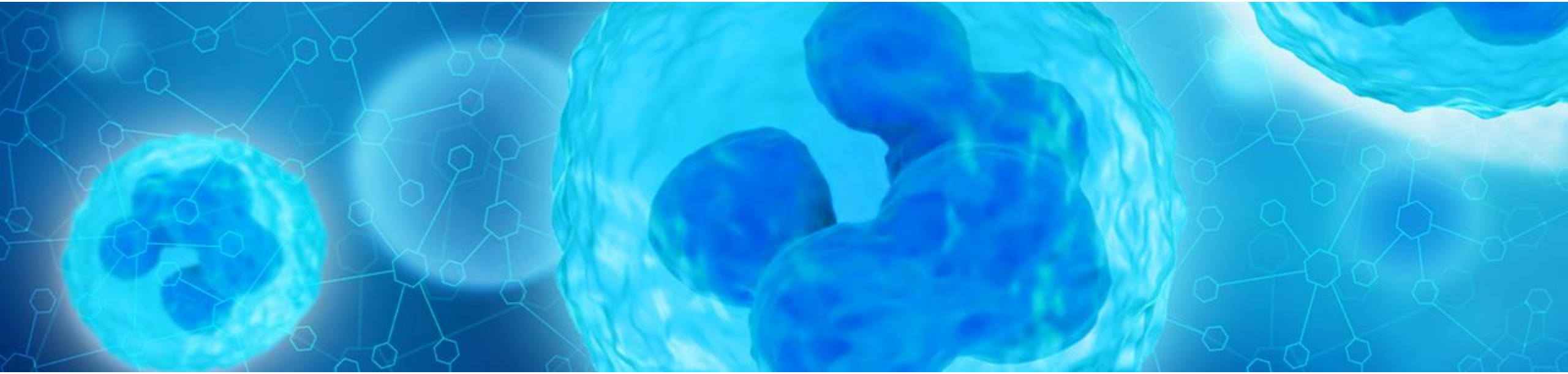
- **Broad anti-inflammatory activity**
  - MP1032 acts **upstream** of **multiple inflammatory pathways (cytokines, kinases, mitochondrial dysfunctions, senescent cells)**
  - For example, **cytokines are broadly downregulated to physiological levels - but not below physiological levels**
  - MP1032 shows **strong anti-inflammatory activity similar to corticosteroids** - but **without serious side effects**
  - MP1032 **synergistically enhances the efficacy** of other anti-inflammatory therapeutics, e.g. **corticosteroids**, **DMF (Tecfidera®)**

Summary (2)
Platform of Oral Modulators Targeting the Mitochondrial Metabolism in Macrophages

- **Host-directed antiviral and antibacterial activity**
  - -> Broad **host-directed** & **dose-dependent antiviral activity** against **6 tested variants of COVID**
  - -> **Host-directed antiviral activity also** against other **RNA-based viruses (**e.g. **RSV, Influenza)**
  - -> Strong **host-directed antibacterial activity** against **several tested bacterial strains including multidrug-resistant strains**
  - -> **Host-directed therapy** is a promising approach for treating **antibiotic-resistant bacterial strains**

- **Excellent safety profile** - especially **no immunosuppression**
  - -> **Dose-limiting toxicity could not be reached –** even though up to **1,000 times the human dose** has been administered
  - -> **Not a single drug-related serious adverse event** was observed in **4 clinical** trials with **366 patients** (**234 verum** + 132 placebo)
  - -> **Fewer treatment-emerging adverse events** (non-drug related) in the **treatment groups versus placebo** (dose-dependent!)

- **Strong intellectual property portfolio**
  - -> **21 patent families** including **98 granted patents**
  - -> Additional **medical use patents pending valid until 2042/2043**

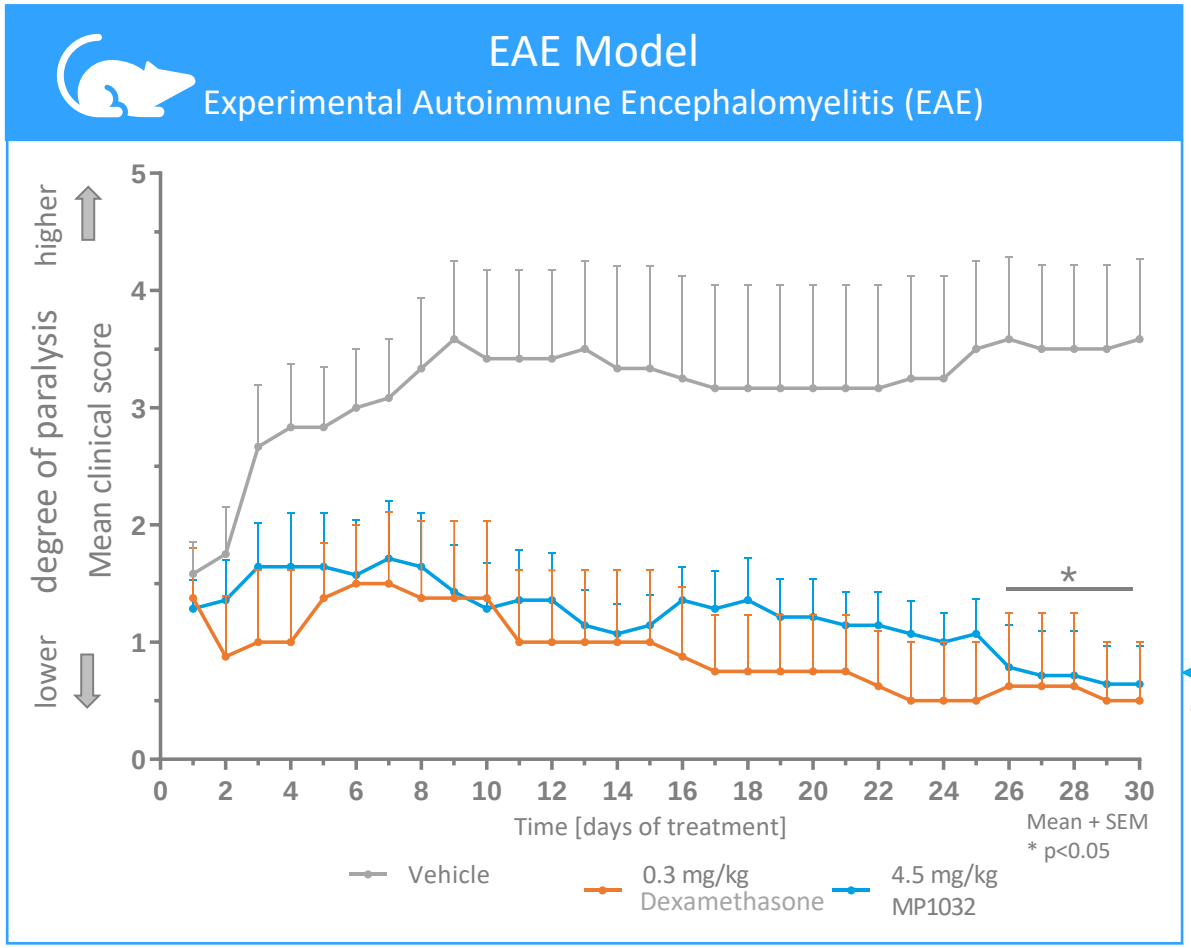


APPENDIX

Selection of Efficacy Studies in Inflammatory and Infectious Diseases

Pre-Clinical : Multiple Sclerosis EAE Model

Multiple Sclerosis



Placebo = Paralysis

MP1032 = No Disease Progression

Dexamethasone (corticosteroid)

Study conducted by Prof. Nicoletti, University of Catania, Italy

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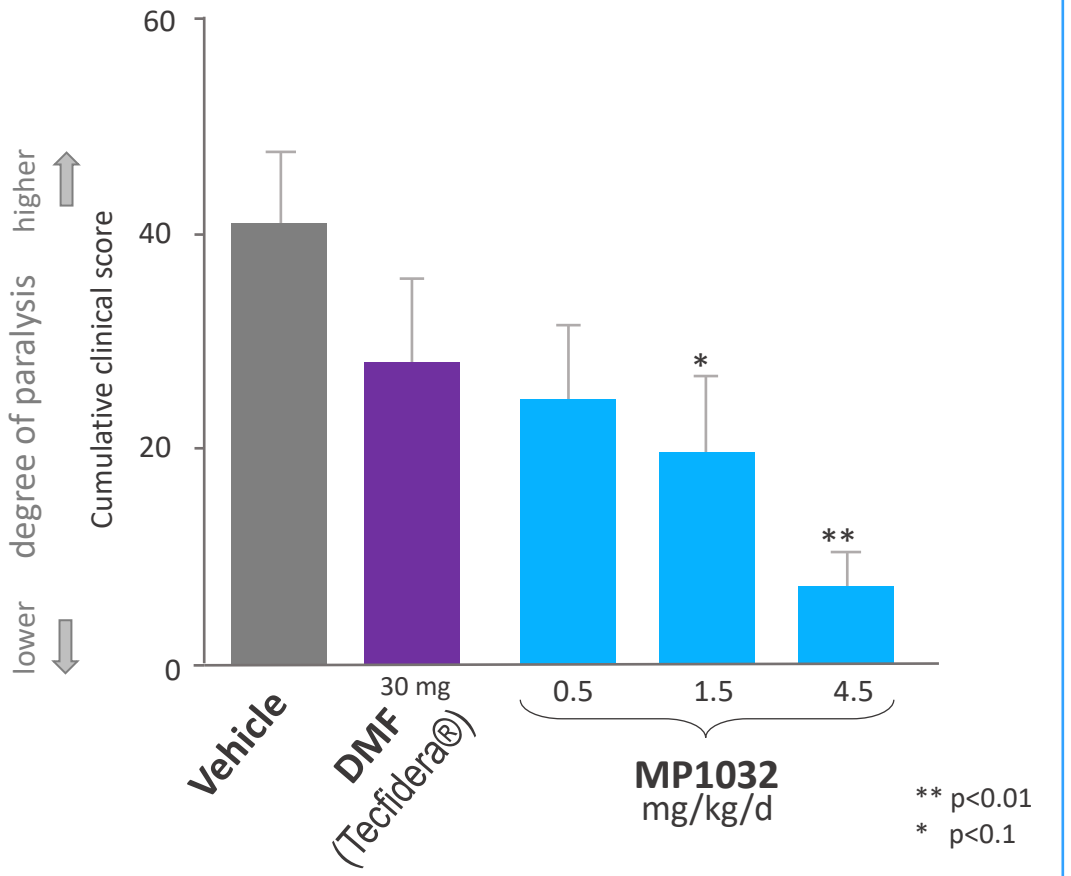
MP1032 works better than leading oral MS drug

MS

EAE model

MP1032 comparison to leading standard of care: DMF

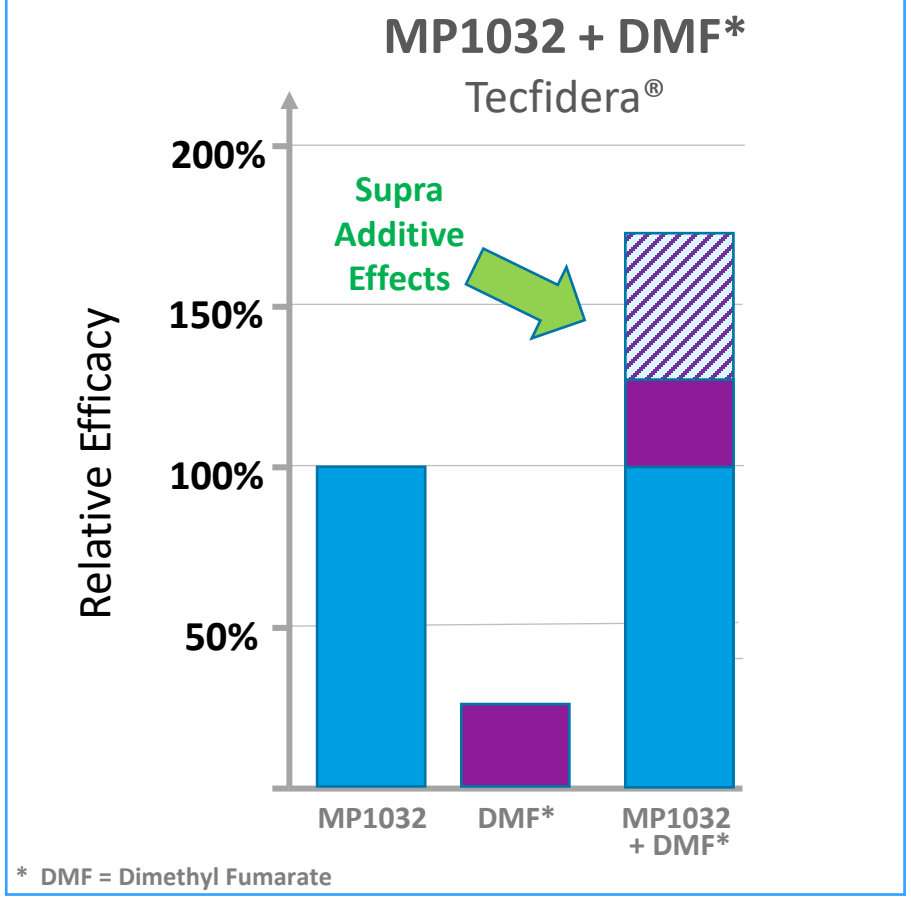


Study conducted by Prof. Nicoletti, University of Catania, Italy

Synergism with Best-in-Class Potential for MS

Cumulative Inhibition of Cytokines

IL-6 IL17a/f TNF-α



BioMap Assay performed by Eurofins

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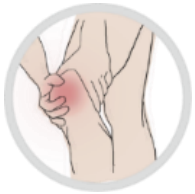


Rheumatoid Arthritis

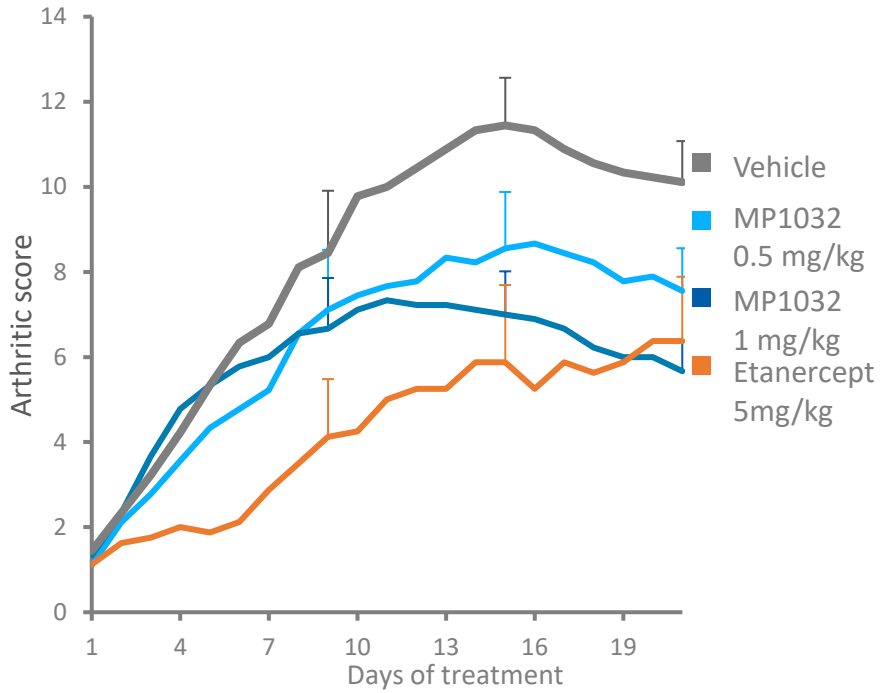
Pre-Clinical POC: Rheumatoid Arthritis (1)

MP1032 improves Arthritic Disease Score and Joint Preservation in CIA Model

Collagen-Induced Arthritis (CIA) mouse model

Improvement of arthritic score

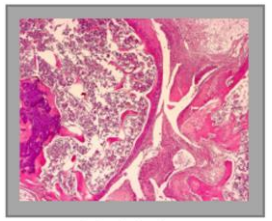
- lower is better -



In Collagen-induced arthritis (CIA) mouse model, MP1032 treatment resulted in significantly improved arthritic disease score, **on par with TNF-inhibitor Etanercept (Enbrel®).**

Knee Joint Histology Cross-sections (day 20)

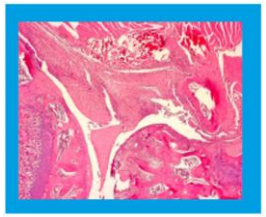
Placebo



Vehicle

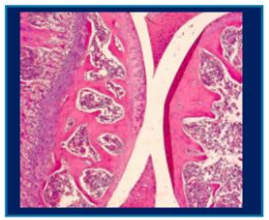
Cross section of hind-leg knee joint, showing massive infiltration and destruction of jont morphology

MP1032



0.5 mg/kg

Low-dose MP1032 results in less infiltration and partial joint preservation.



1.0 mg/kg

High-dose MP1032 results in minor infiltration and complete joint preservation.

Histological assessment showed dose-dependent disease modifying effect in form of joint preservation.

Studies performed by Prof. Nicoletti, University of Catania, Italy

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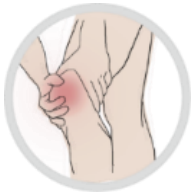


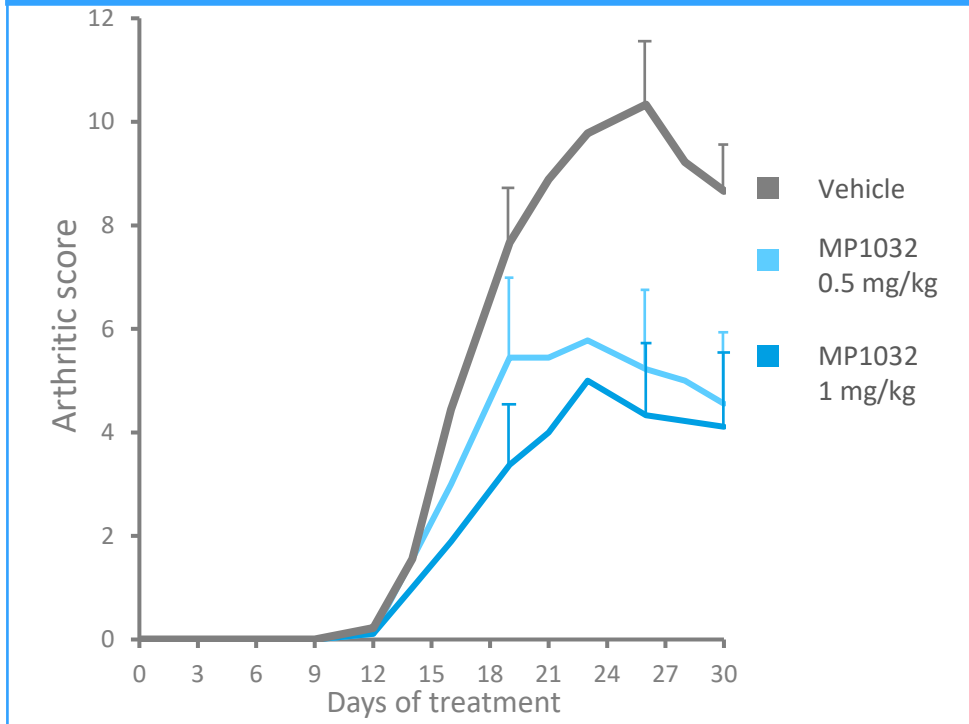
Rheumatoid Arthritis

Pre-Clinical: Rheumatoid Arthritis Model (2)

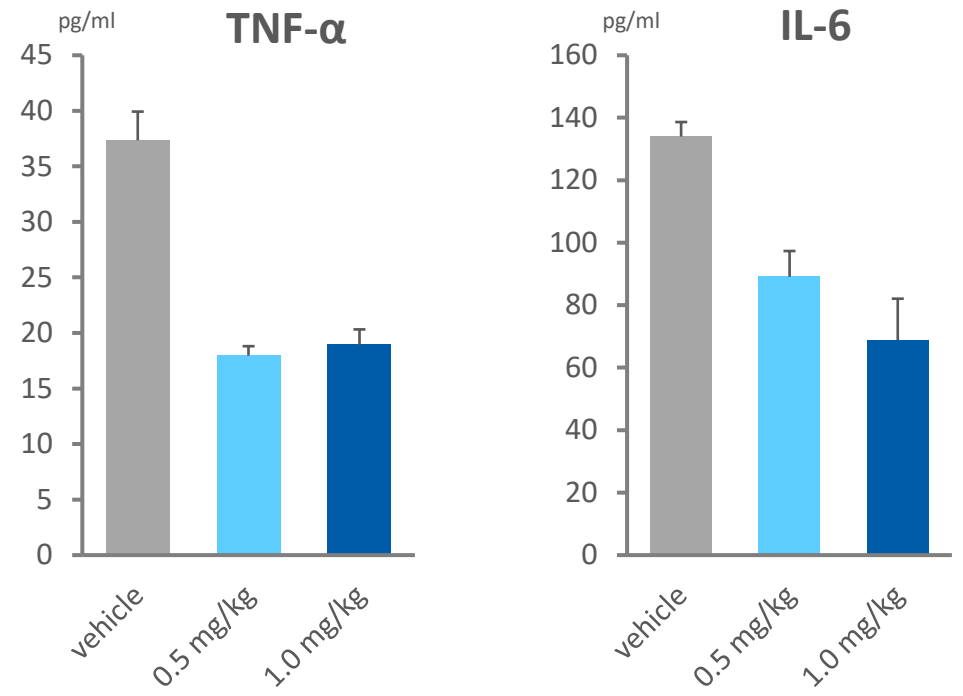
Antigen-Induced Arthritis (AIA) mouse model

Improvement of Arthritic Score

- lower is better -



Cytokine Inhibition (day 23)



In this antigen-induced arthritis (AIA) mouse model, MP1032-mediated immune metabolic modulation improved arthritic disease score compared to vehicle.

MP1032 induced a significant inhibition of two key pro-inflammatory cytokines involved in auto-immune arthritis in mouse AIA model.

Studies performed by Prof. Nicoletti, University of Catania, Italy

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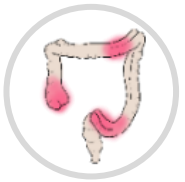


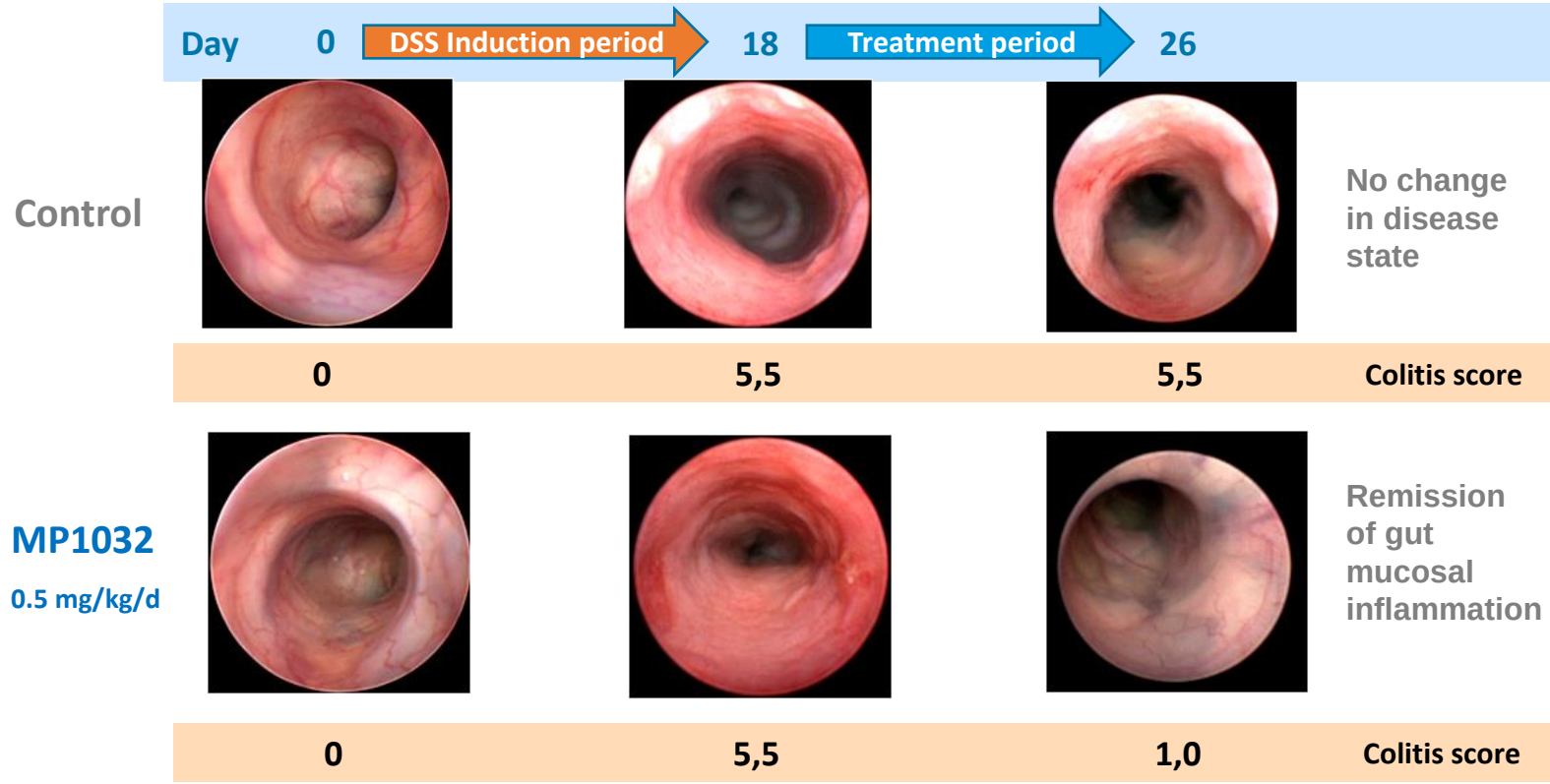
Crohn's
U. Colitis

Pre-clinical POC: Inflammatory Bowel Disease

MP1032-mediated metabolic modulation improves gut inflammation in DSS-induced Colitis Mouse Model

DSS-induced Colitis MouseModel

Endoscopic images from colon



In DSS-induced colitis mouse model. Systemic once-daily treatment with MP1032 metabolic modulator after full induction (therapeutic treatment) resulted in a near-complete remission of gut mucosa within 8 days. Endoscopic images of colon.

Study perfomed by Dr. Grötzinger, Charité, Berlin, Germany

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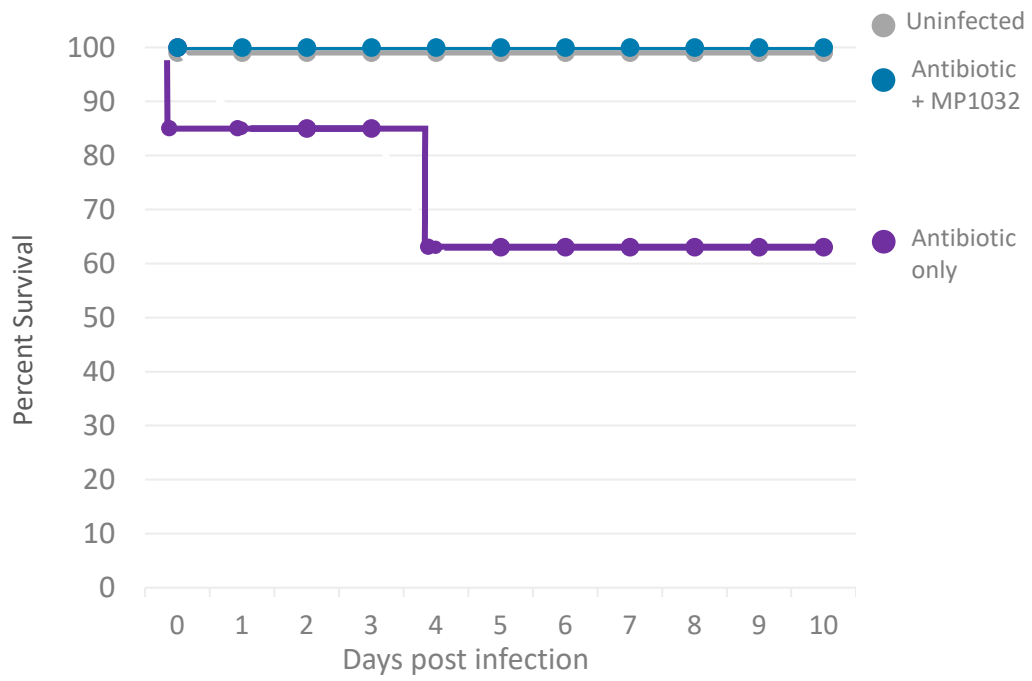
Bacterial Infection
Sepsis

Preclinical POC: Sepsis (1)

Feces-Injection Peritonitis Model (Mouse)

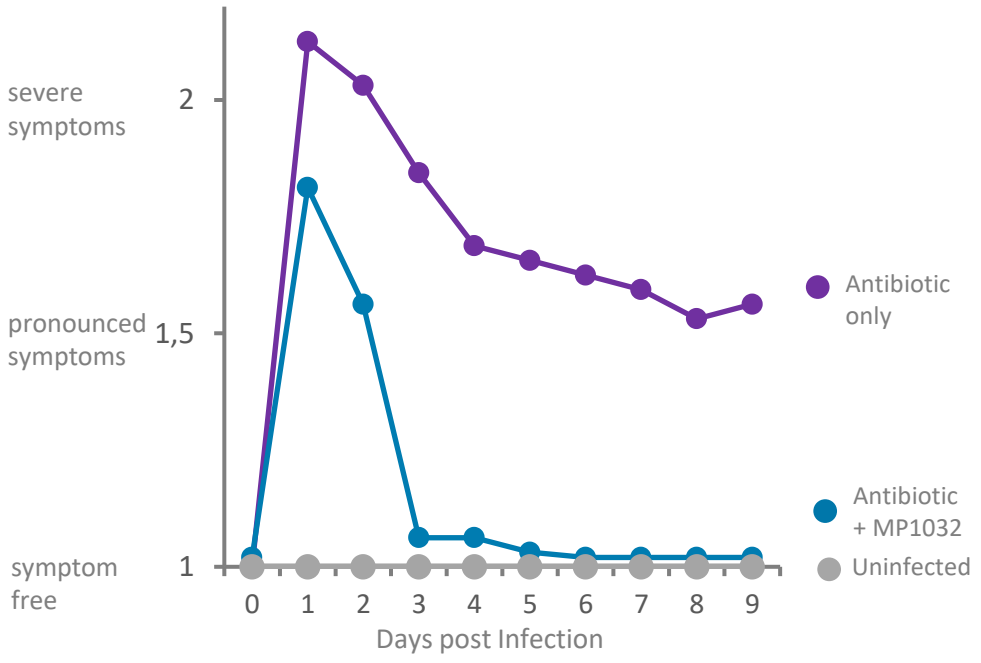
10-Day Survival of Severe Sepsis

Standard Antibiotic treatment vs. Antibiotic + MP1032 combination



Clinical State and Recovery Time

Standard Antibiotic treatment vs. Antibiotic + MP1032 combination



100% animals treated with antibiotic Meropenem plus MP1032 combination therapy survived and fully recovered.
62% of animals in the Meropenem-only group survived, albeit in a clinically poor condition.

The Gonnert score evaluates clinical and behavioral signs of disease and health in animals: movement vs. apathy; food intake, fur, stool. Ranges from 1.0 (normal/healthy) to 3.0 (terminally ill).
Animals treated with antibiotic + MP1032 combination fully recovered within 3 days. Surviving animals treated with antibiotic monotherapy recovered only partially.

Double-blinded study performed by Dr. Ignazio Rubio, Center for Sepsis Control and Care, Jena, Germany

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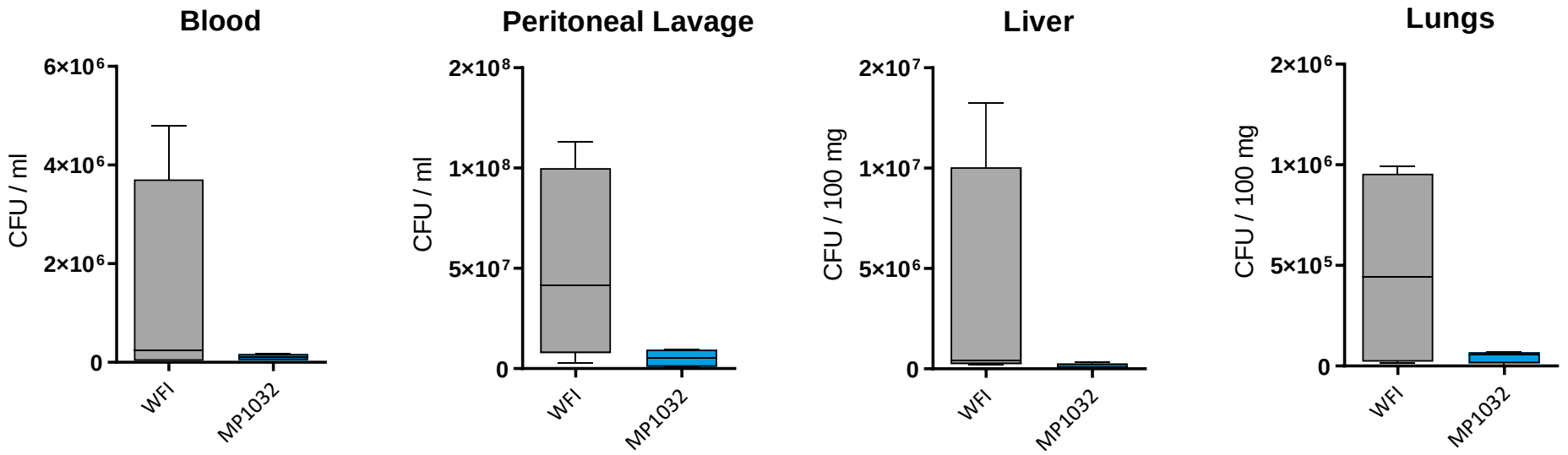
Bacterial Infection
Sepsis

Preclinical POC: Sepsis (2)

Host-Directed Anti-Bacterial Effect of MP1032 Metabolic Modulation

Colon Ascendens Stent Peritonitis (CASP) Sepsis Model

Anti-bacterial effect of MP1032-mediated Macrophage Metabolic Modulation



Number of bacteria (CFU = colony forming units) in different tissues 12 hours after CASP peritonitis induction. Animals were treated with two systemic doses of MP1032, 1h and 7h post sepsis induction as sole treatment. Water for injection (WFI) was used as control.

This marked **anti-bacterial effect was mediated solely by MP1032 Macrophage Metabolic Modulation**, since direct treatment of bacterial cultures with MP1032 had no influence on bacterial growth (data not shown). Consequently, redox metabolic modulation is a **highly promising approach to treat bacterial infections** that also covers **all antibiotic-resistant strains**.

Study performed by Prof. Traeger, University of Greifswald, Germany

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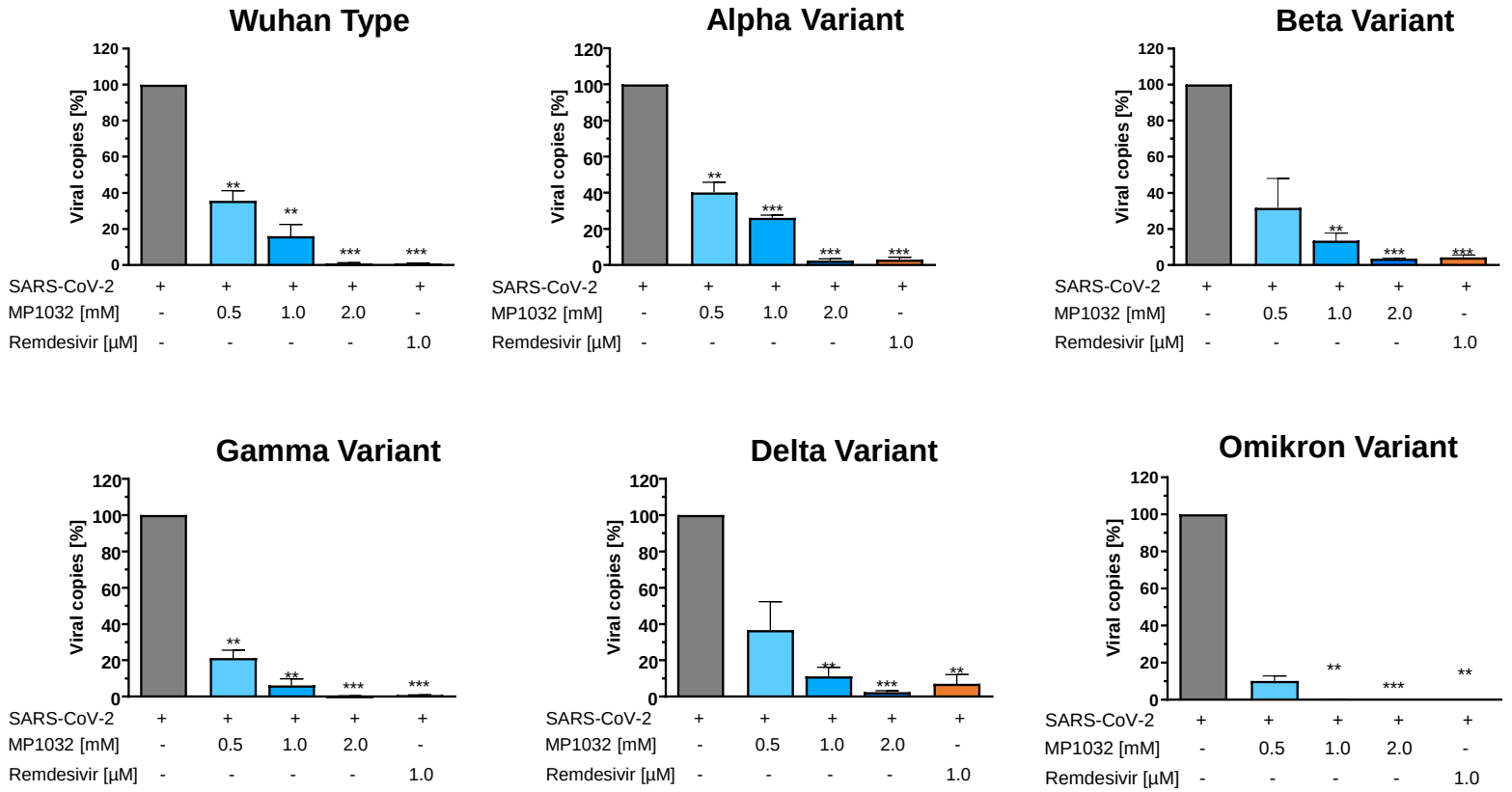
Anti-Viral Activity of MP1032 Against Various SARS-CoV-2 Variants

Host-Directed & Dose Dependent Efficacy - Independent from Virus Variants

COVID-19

MP1032: SARS-CoV-2 Viral Replication in Human Lung Epithelial Cells



Human lung epithelial cells were infected with virus variants of SARS-CoV-2. Virus replication was reproducibly reduced by MP1032 in dose-dependent manner. Anti-viral effect was consistent, independent of virus variant.

Data from Schumann S et al. Immune-Modulating Drug MP1032 with SARS-CoV-2 Antiviral Activity In Vitro: A potential Multi-Target Approach for Prevention and Early Intervention Treatment of COVID-19. Int J Mol Sci. 2020 Nov 20;21(22):8803. Further data from ImmunoLogik GmbH in collaboration with Prof. Ulrich Schubert of University of Erlangen, Germany.

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COVID-19[1] Phase IIa Study Final Data Analysis
PoC for Host-Directed Therapies for Potentially Pandemic Infectious Diseases[1]

Final data analysis reveals significantly better results than early top-line data suggested

Efficacy and safety advantages compared to Standard of Care (SoC)[2]:

- Hospitalization times **reduced by 2.4 days**
  (Better than published data of existing drugs Remdesivir and Molnupiravir at similar endpoints)
- Median Intensive-Care-Unit-stay: **4 days shorter**
- **23% lower** relative long-term (60d) mortality
- **Favorable biomarker** readouts compared to placebo + SoC
  - Lower C-Reactive Protein (CRP) => lower general inflammation
  - Higher GFR => better kidney function (predictor of better clinical outcomes)

[1] Phase IIa study was financed by **EU grant of EUR7.9m**; data were published in ***Lancet Regional Health (Europe);*** this study could serve as PoC for **Host-Directed** Therapies for potentially pandemic infectious diseases such as **COVID, RSV, Influenza** ("**Pandemic Preparedness**")

[2] **Findings from MP1032 treatment group + SoC compared to placebo group + SoC as calculated by Saarmetrics**

USA: Medical Need and Government COVID Therapeutics Strategy

ASPR Administration for Strategic Preparedness & Response

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY BARDA

Outpatient

PrEP	PEP	Therapy
No Illness	Exposed Per CDC Close Contact Criteria	COVID ++ Mild to Moderate Symptoms

Pre-Exposure Prophylaxis (PrEP)

- No approved PrEP treatment available
- „Evusheld“ not authorized for emergency use anymore (FDA)

Post-Exposure Prophylaxis (PEP)

- No current PEP treatments
- Studying new and improved treatments a virus variants change

COVID-19 Treatment

Effective when started within a specific limited timeframe from onset of illness

- Oral antiviral
- IV antiviral
- Monoclonal antibodies (mAbs)

Paxlovid Lagevrio (molnupiravir)

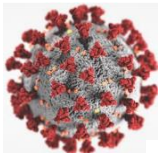
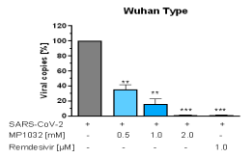
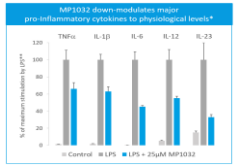
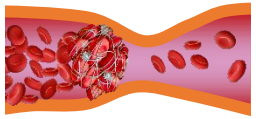
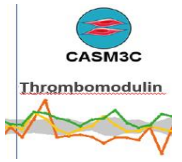
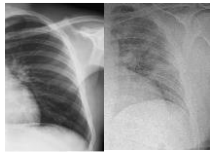
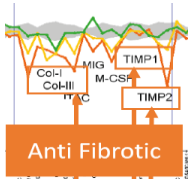
MP1032 COVID Market Opportunity

Still no approved drug available for these market segments

MP1032 is Effective Against 4 Cardinal Drivers of Long COVID

MP1032 Immune-Metabolic Modulation: A Multi-modal Therapy Opportunity to Treat Long COVID

COVID-19

Long Covid Pathology	References	MP1032 Therapeutic Effect
1 Persistent Virus 	Couzin-Frankel J. Clues to long COVID. Science. 2022 Jun 17;376(6599):1261-1265 Zollner A, Koch R, et al. Postacute COVID-19 is Characterized by Gut Viral Antigen Persistence in Inflammatory Bowel Diseases. Gastroenterology. 2022 Aug;163(2):495-506	 MP1032 inhibits SARS-CoV-2 replication independent of virus variants **MP1032 Effect** Fights persistent virus
2 Immune Metabolic Dysregulation  TNF-α ↑ IL-1β ↑ IL-6 ↑	Phetsouphanh C, Darley DR, et al. Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. Nat Immunol. 2022 Feb;23(2):210-216. Schultheiß C, Willscher E, et al. The IL-1β, IL-6, and TNF cytokine triad is associated with post-acute sequelae of COVID-19. Cell Rep Med. 2022 Jun 21;3(6):100663	 MP1032 inhibits pathologic cytokine release **MP1032 Effect** Normalization of persistent immune dysregulation
3 Micro Embolisms 	Buonsenso D, Di Giuda D, et al. Evidence of lung perfusion defects and ongoing inflammation in an adolescent with post-acute sequelae of SARS-CoV-2 infection. Lancet Child Adolesc Health. 2021 Sep;5(9):677-680.	 MP1032 induces the endogenous factor thrombomodulin **MP1032 Effect** Prevention of micro-embolisms
4 Lung Fibrosis  Normal COVID	Mohammadi A, Balan I, et al. Post-COVID-19 Pulmonary Fibrosis. Cureus. 2022 Mar 2;14(3)	 MP1032 inhibits fibrotic biomarkers **MP1032 Effect** Inhibits pulmonary fibrosis

Long COVID is emerging as a multi-facetted systemic disease which shows the typical hallmarks of pathologic macrophage re-programming. This has detrimental effects on a number of different organ systems. MP1032-mediated macrophage metabolic modulation is a drug mechanism that broadly targets the diverse causes and symptoms of Long Covid. The high unmet medical need and lack of approved therapeutics for Long Covid makes this a highly promising and attractive target indication for MP1032.

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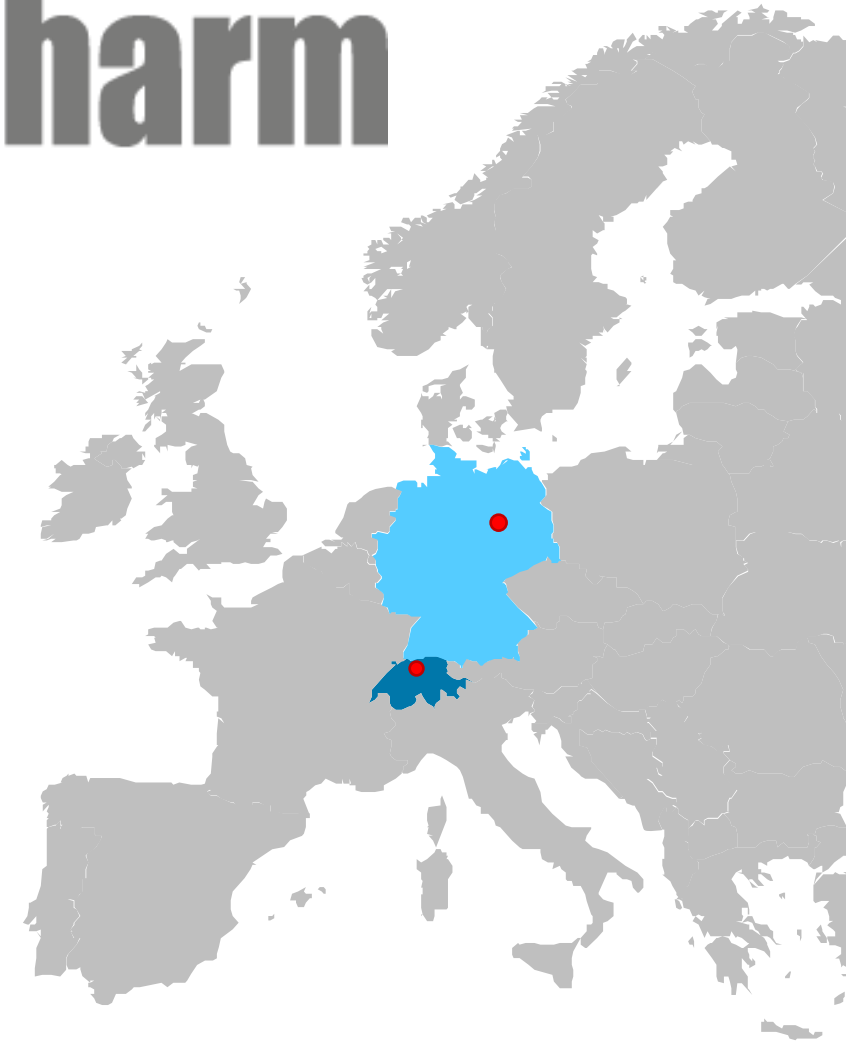
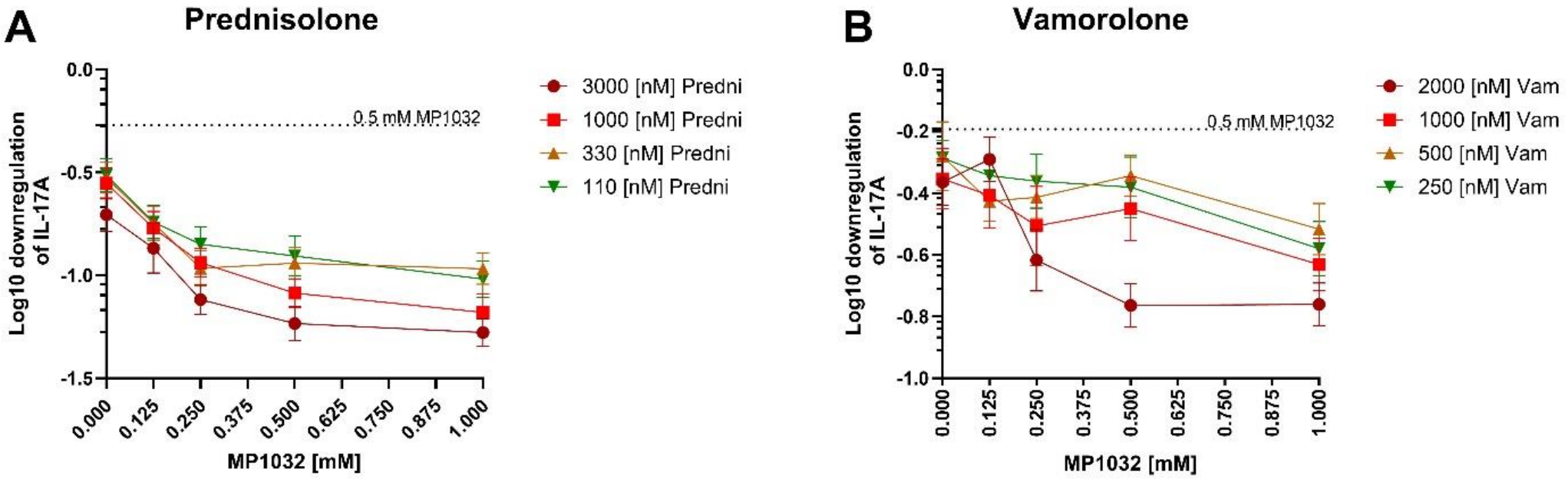


MP1032 Enhances Corticosteroid-Induced Reduction of Inflammatory Cytokine IL-17A



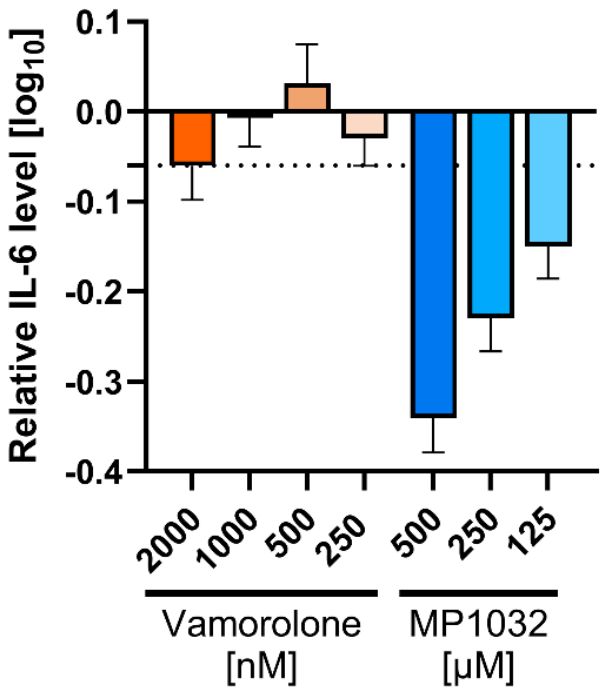
BioMap BioMAP BT Cell System performed by Eurofins

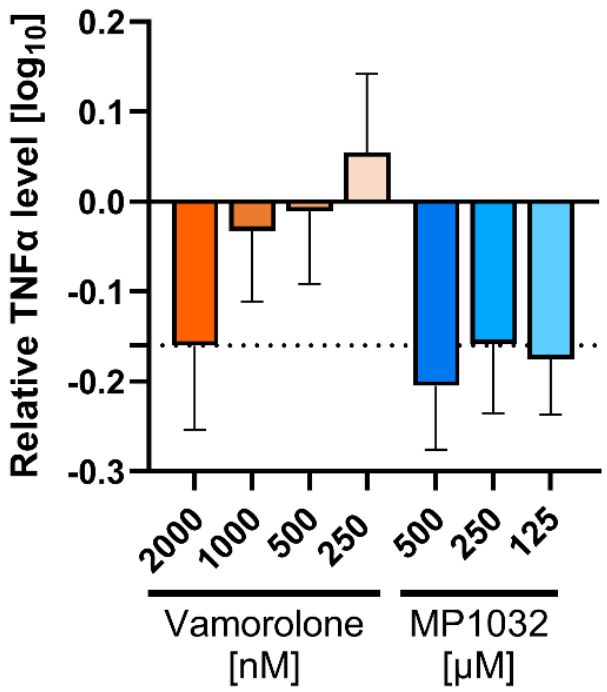
MP1032 enhances Corticosteroid anti-inflammatory potency

Addition of MP1032 to Prednisolone or Vamorolone reduced levels of inflammatory cytokines IL-17A, supporting its corticosteroid-sparing effect. IL-17A is associated with DMD.

MP1032 Reduces IL-6 and TNF-α Stronger Than Vamorolone

MP1032 vs. Vamorolone: Reduction of Pro-Inflammatory Cytokines





BioMap
BT Cell System Assay
performed by Eurofins

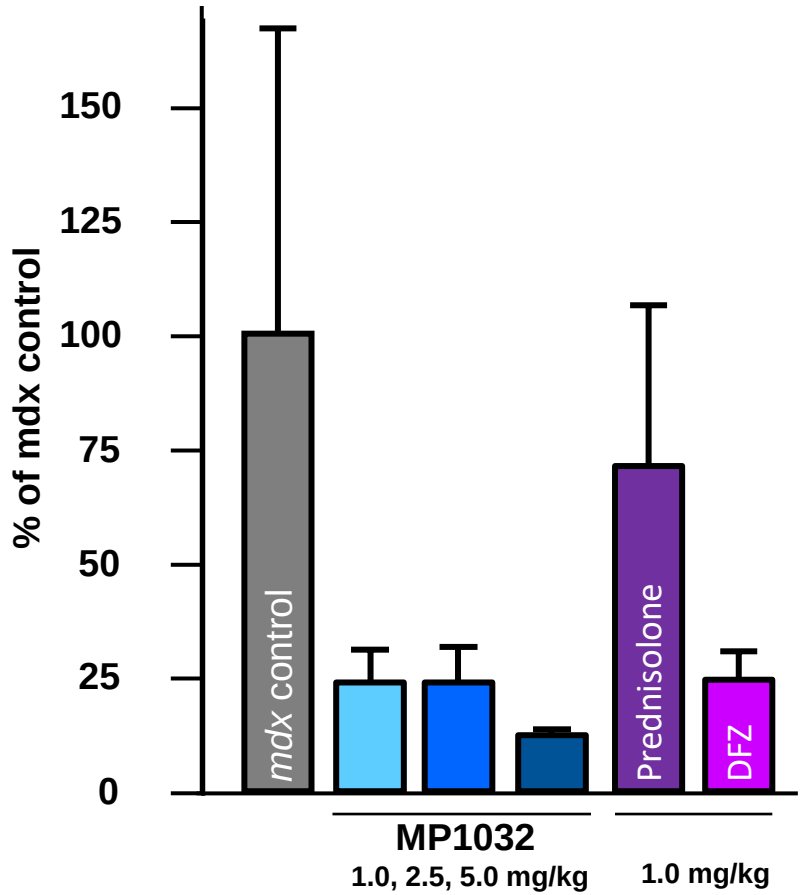
Superior anti-inflammatory effect than Vamorolone

MP1032 reduces levels of inflammatory cytokines IL-6 and TNFα in stimulated human cells stronger than corticosteroid Vamorolone.

MP1032 Has Stronger Anti-Inflammatory Effects Than Corticosteroids

in DMD Animal Model (mdx mice)

Histological Inflammation in Muscles



Less inflammatory foci in muscles

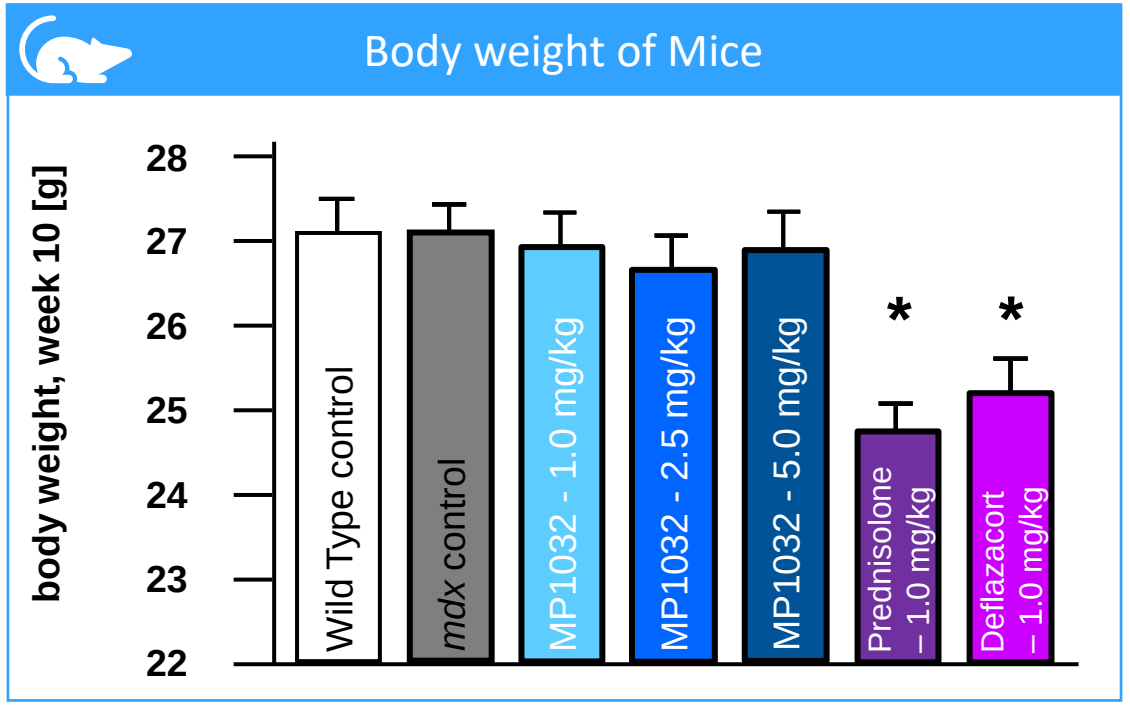
mdx mice treated with MP1032 showed less histological inflammatory foci in TA* muscle than *mdx* mice treated with Prednisolone or Deflazacort.

* TA = Tibialis Anterior

Study performed by Agada Research Ltd., Halifax, Canada

Example: MP1032 Has Less Side Effects than Corticosteroids

in DMD Animal Model (mdx mice)



Study performed by Agada Research Ltd. Halifax, Canada

MP1032 lacks growth-related side effects of corticosteroids

mdx mice treated with MP1032 showed normal growth - compared to impaired body weight development of corticosteroid treated mice.