Corporate Presentation, Q4-2022

ZyVersa THERAPEUTICS℠

Restoring Health, Transforming Lives Through Innovation

Disclaimer (1 of 2)

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Additional Information

In connection with the Business Combination, Larkspur intends to file with the U.S. Securities and Exchange Commission’s (“SEC”) a Registration Statement on Form S-4 (the “Registration Statement”), which will include a preliminary prospectus and preliminary proxy statement. Larkspur will mail a definitive proxy statement/final prospectus and other relevant documents to its stockholders. This communication is not a substitute for the Registration Statement, the definitive proxy statement/final prospectus or any other document that Larkspur will send to its stockholders in connection with the Business Combination. Investors and security holders of Larkspur are advised to read, when available, the proxy statement/prospectus in connection with Larkspur’s solicitation of proxies for its special meeting of stockholders to be held to approve the Business Combination (and related matters) because the proxy statement/prospectus will contain important information about the Business Combination and the parties to the Business Combination. The definitive proxy statement/final prospectus will be mailed to stockholders of Larkspur as of a record date to be established for voting on the Business Combination. Stockholders will also be able to obtain copies of the proxy statement/prospectus, without charge, once available, at the SEC’s website at www.sec.gov or by directing a request to: 100 Somerset Corporate Blvd., 2nd Floor Bridgewater, New Jersey.

Participants in the Solicitation

Larkspur, ZyVersa and their respective directors, executive officers, other members of management, and employees, under SEC rules, may be deemed to be participants in the solicitation of proxies of Larkspur’s stockholders in connection with the Business Combination. Investors and security holders may obtain more detailed information regarding the names and interests in the Business Combination of Larkspur’s directors and officers in Larkspur’s filings with the SEC, including the Registration Statement to be filed with the SEC by Larkspur, which will include the proxy statement of Larkspur for the Business Combination, and such information and names of ZyVersa’s managers and executive officers will also be in the Registration Statement to be filed with the SEC by Larkspur, which will include the proxy statement of Larkspur for the Business Combination.

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Cautionary Statement Regarding Forward Looking Statements

This presentation contains certain forward-looking statements within the meaning of the federal securities laws with respect to the proposed transaction between Larkspur and ZyVersa. All statements other than statements of historical facts contained in this presentation, including statements regarding Larkspur or ZyVersa's future results of operations and financial position, the amount of cash expected to be available to ZyVersa after the closing and giving effect to any redemptions by Larkspur's stockholders, ZyVersa's business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations, future results of current and anticipated products, and expected use of proceeds, are forward-looking statements. These forward-looking statements generally are identified by the words "believe," "project," "expect," "anticipate," "estimate," "intend," "strategy," "future," "opportunity," "plan," "may," "should," "will," "would," "will be," "will continue," "will likely result," and similar expressions. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to, the following risks relating to the proposed transaction: the risk that the transaction may not be completed in a timely manner or at all, which may adversely affect the price of Larkspur's securities; the failure to satisfy the conditions to closing the transaction, including the approval by the stockholders of Larkspur or ZyVersa and the receipt of certain governmental and regulatory approvals; the risk that some or all of Larkspur's stockholders may redeem their shares at the closing of the transaction; the effect of the announcement or pendency of the transaction on ZyVersa's business relationships and business generally; the outcome of any legal proceedings that may be instituted related to the transaction; the ability to realize the anticipated benefits of the transaction; ZyVersa may use its capital resources sooner than it expects; and the risks associated with ZyVersa's business set forth in this presentation. Moreover, ZyVersa operates in a very competitive and rapidly changing environment. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond Larkspur's and ZyVersa's control, you should not rely on these forward-looking statements as predictions of future events. Forward-looking statements speak only as of the date they are made. Readers are cautioned not to put undue reliance on forward-looking statements, and except as required by law. Larkspur and ZyVersa assume no obligation and do not intend to update or revise these forward-looking statements, whether as a result of new information, future events, or otherwise. Neither Larkspur nor ZyVersa gives any assurance that either Larkspur or ZyVersa or the combined company will achieve its expectations.

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Industry and Market Data

Information contained in this presentation concerning the market and the industry in which ZyVersa competes, including its market position, general expectations of market opportunity and market size, is based on information from various third-party sources, on assumptions made by ZyVersa based on such sources and ZyVersa's knowledge of the markets for its services and solutions.

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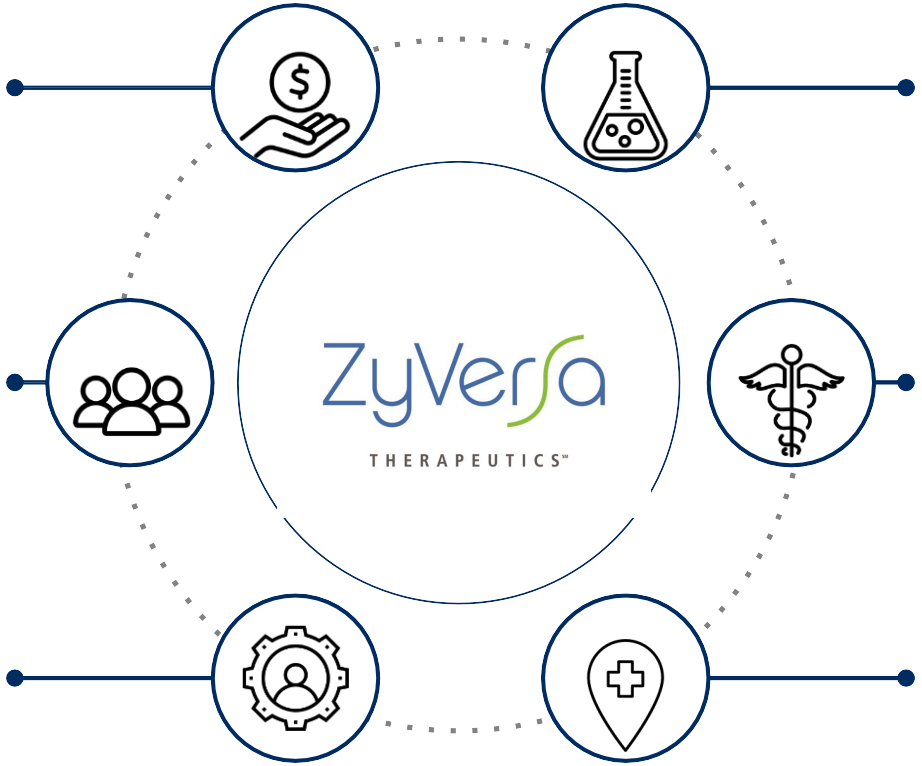
ZyVersa's Value Proposition

With two exciting programs in attractive areas, ZyVersa is well positioned to drive shareholder value over the next 12-18 months

~$75 billion global total addressable inflammatory and renal disease markets[1] [2]

CEO co-founded & led multiple biopharma companies & built current management team with successful leaders from his prior companies

Strong Board of Directors and globally renowned scientific advisors



Two proprietary product platforms invented by top tier research scientists at University of Miami Miller School of Medicine

Orphan disease-focused Phase 2a drug candidate leading a robust renal pipeline

Highly differentiated mAb targeting inflammasome ASC to block initiation & perpetuation of damaging inflammation

1. Chronic Kidney Disease Drugs Market Analysis. Coherent Market Insights, November 2020; 2. Anti-Inflammatory Biologics Market Size, Share & Industry Analysis. Fortune Business Insights, May 2020

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ZyVersa Investor Highlights

2 Proprietary Product Platforms	• Anti-inflammatory and renal platforms each offer a "pipeline in a product" • Multiple potential indications in both categories target over $75B TAM
Renal VAR 200 Cholesterol Efflux Mediator	• Differentiated MOA: Mediates removal of excess intracellular lipids that contribute to kidney damage and dysfunction • Renal orphan focused • Safety profile enabling FDA clearance for Phase 2 • Next catalysts: Initiate IIT study in renal patients for human proof-of-concept
Anti-inflammatory IC 100 Inflammasome Inhibitor	• mAb designed and engineered by leading inflammasome and monoclonal antibody experts • Differentiated MOA: ASC inhibition attenuates initiation and perpetuation of inflammation • Preclinical pharmacology supports IND indications in MS and ARDS • Initial preclinical safety established; small scale manufacturing completed • Opportunity for indication expansion: Parkinson's disease, atherosclerosis, early Alzheimer's disease diabetic nephropathy, atrial fibrillation, systemic lupus, lupus nephritis, heart failure, certain cancers • Next catalysts: GLP tox study for IND and cGMP manufacturing
Inflammasome Opportunity	• Positioned in rapidly emerging inflammasome space; mAb providing a highly differentiated MOA • Highly attractive to biopharma and investors; over $4B in M&A activity for preclinical/phase 1 programs over last 18 months in this sector (acquisitions by Roche, Novartis and BMS)[(1)]

Proven Leadership Team and SAB	• CEO co-founded & led multiple biopharma companies & has successful track record in licensing, M&A, raising capital, and taking companies public
	• Current management team built from successful leaders from CEO's prior companies
	  - Prior experience at Roche, Amgen, Novartis, Abbott, Genentech and J&J
	  - Led development of numerous top biologics through approval
	• SAB members are renowned leaders in inflammasome and renal research
	  - Drs. Barbosa and Baker are Former global Heads of Immunology Research at J&J

1. Pitchbook as of 12/2/20

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Highly Experienced Leadership Team

Stephen C. Glover

- Co-Founder, Chief Executive Officer, and President
- Over 38 years in biopharmaceuticals and life sciences
- Previous roles at Coherus Biosciences, Insmed, Andrx, Amgen, and Roche
- Serves on the Boards of PDS Biotechnology, The Coulter Foundation (University of Miami), and Asclepius Lifesciences

Pablo A. Guzman, MD, FACC

- Consultant/Acting Chief Medical Officer and Chairman, Renal Scientific Advisory Board
- Over 40 years in medicine
- Previous roles at American College of Cardiology, Johns Hopkins University, and Holy Cross Hospital
- Serves on the Boards of North Ridge Medical Center and Holy Cross Hospital

Peter Wolfe

- Senior Vice President, Finance and Administration
- Over 20 years in biopharmaceuticals and life sciences
- Previous roles at KOS and Noven Pharmaceutials

Nick A. LaBella, MS, RPH

- Chief Scientific Officer, Senior VP Research and Development
- Over 34 years in biopharmaceuticals and life sciences
- Previous roles at Insmed, Cardiokine, Watson Laboratories, and Sandoz

Karen Cashmere

- Chief Commercial Officer
- Over 30 years in biopharmaceuticals and life sciences
- Previous roles at Abbott (now AbbVie), EMD Serono, Noven/Novartis Joint Venture, Andrx, and Auxilium

Melda Uzbil O'Connell

- Consultant/Acting Senior Vice President, Corporate Development
- Over 17 years in academic technology commercialization, business development and fund raising
- Previous roles at Pfizer, Duke and State of Michigan

Deep pharmaceutical experience and successful track record

>35 NDA/BLA Filings, >55 New Product Launches, >15 rare disease indications, >40 Licensing Deals & Acquisitions
$10B+ of Licensing and M&A experience, Over $250M of Private Capital Raised

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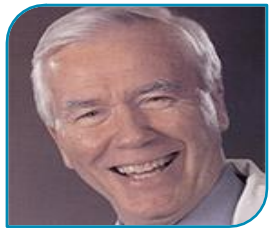
Top Tiered Renal Scientific Advisory Board, Known for Leadership in Glomerular Research and Advocacy

Sharon G. Adler, MD

- Professor of Medicine, David Geffen School of Medicine, UCLA
- Chief, Division of Nephrology and Hypertension, Harbor-UCLA Medical Center
- Program Director, Nephrology Fellowship Training Program, Harbor-UCLA Medical Center



Daniel C. Cattran, MD

- Professor of Medicine, University of Toronto
- Chair of the Toronto Glomerulonephritis Registry

Fernando C. Fervenza

- Professor of Medicine, Mayo Graduate School of Medicine
- Director, Nephrology Collaborative Group

Alessia Fornoni MD, PhD

- Professor of Medicine and Chief, Katz Family Division of Nephrology and Hypertension, University of Miami Miller School of Medicine

Pablo A. Guzman, MD, FACC

- Chairman, Scientific Advisory Board
- Chief Medical Officer, ZyVersa Therapeutics

Debbie S. Gipson, MD, MS

- Professor, Department of Pediatrics, University of Michigan
- Director, Kidney Research Network Coordinating Center

Marlene Haffner, MD, MPH

- Principal & Founder, Orphan Solutions & Haffner Associates
- Former Director of Orphan Products Development, FDA

Renowned Anti-inflammatory Scientific Advisory Board, Recognized As Pioneers/Leaders in Inflammasome Inhibitor Space

Miguel S. Barbosa, PhD

- Former Global Head and Vice President of Immunology Research and External Innovation at Janssen Research & Development, Pharmaceutical Companies of Johnson & Johnson

Daniel G. Baker, MD

- Former Vice President, Immunology Research and Development, Janssen Pharmaceutical Companies of Johnson & Johnson

Doug H. Farrar

- CEO, Flatirons Biotech, Inc
- Former Cofounder and Chief Technical Officer, Coherus Biosciences
- Former SVP biologic manufacturing at Amgen and Insmed

Alan Herman, PhD

- Chairman Emeritus, former Chief Scientific Officer, Coherus Biosciences
- Formerly: Genentech, Amgen, Merck, Coherus Biosciences

William F. Bennett, PhD

- Principal, Bioscope Associates
- Formerly: Genentech, Sensus Corporation, Cor Therapeutics

Robert W. Keane, PhD: Inventor of Inflammasome Platform

- Professor Physiology & Biophysics, Neurological Surgery & Microbiology, and Immunology, UM
- The Miami Project to Cure Paralysis, UM

Juan Pablo de Rivero Vaccari, PhD: Inventor of Inflammasome Platform

- Research Assistant Professor, Department of Neurological Surgery, UM
- The Miami Project to Cure Paralysis, UM
- Distinguished Faculty Member of The Center for Cognitive Neuroscience and Aging, UM

W. Dalton Dietrich, III, PhD: Inventor of Inflammasome Platform

- Kinetic Concepts Distinguished Chair in Neurosurgery & Scientific Director, The Miami Project to Cure Paralysis, UM
- Senior Associate Dean, Discovery Science & Co-director, Institute for Neural Engineering, UM
- Professor, Neurological Surgery, Neurology, Biomedical Engineering & and Cell Biology, UM

Helen Bramlet, PhD: Inventor of Inflammasome Platform

- Professor, Department of Neurological Surgery, UM
- The Miami Project to Cure Paralysis, UM

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Two Proprietary Product Platforms, Each With "Pipeline Within a Product" Potential

ZyVersa's two proprietary platforms target unmet medical needs with unique MOAs; offer multiple opportunities for expansion beyond initial targeted indications

Product	Development	Pre-clinical	Phase 1	Phase 2	Phase 3	NDA/BLA Submission
Renal/Cholesterol Efflux Mediator						
VAR 200-01: FSGS*						
VAR 200-02 : Alport Syndrome*						
VAR 200-03: Diabetic Kidney Disease						
Inflammasome/ASC Inhibitor						
IC 100-01: Acute Respiratory Distress Syndrome*						
IC 100-02: Multiple Sclerosis						
IC 100-03: Parkinson's Disease						
IC 100-04: Pancreatic Cancer*						
IC 100-05: IgA Nephropathy*						
IC 100-06: Huntington's Disease*						
IC 100-O7: Congestive Heart Failure						
IC 100-08: Early Cognitive Impairment						

* Orphan diseases

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Cholesterol Efflux Mediator, VAR 200

2-Hydroxypropyl-Beta-Cyclodextrin (2HPβCD)

VAR 200, Novel Phase 2a-Ready Cholesterol Efflux Program Targeting Orphan Kidney Disease, FSGS

2-Hydroxypropyl-Beta-Cyclodextrin

- Licensed preclinical asset from University of Miami in 2015
- FDA clearance for Phase 2a
- Differentiated MOA: Mediates removal of excess intracellular lipids that contribute to kidney damage and dysfunction; competitive pipeline targets hypertension and inflammation
- Significant Proof of Concept: Pre-clinical data in 3 different animal models of kidney disease (FSGS, Alport syndrome, diabetic kidney disease); safety profile supported by development program and decades of use as excipient
- Lower-risk Opportunity: FDA concurrence to move directly to phase 2a in adults and pediatric patients based on strong pre-clinical program and previous human experience
- IP Protection: 7 years orphan drug exclusivity in US, 10 years in EU; exclusive worldwide license to IP related to 2HPβCD for treatment of kidney diseases
- Opportunity for Indication Expansion: As a cholesterol efflux mediator, offers potential indication expansion across multiple kidney diseases, including Alport syndrome, diabetic kidney disease, and other forms of glomerular disease comprising the global $12B renal market(1)
- Multiple Life Cycle Opportunities

1. Chronic Kidney Disease Drugs Market Analysis. Coherent Market Insights, November 2020

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VAR 200 Positioning and Value Proposition

Expected to be first disease-modifying renal drug addressing pathogenic glomerular lipid accumulation to stop progression of glomerular injury, reduce proteinuria, and delay disease progression

Value Proposition Anticipated

- Induces and maintains partial or complete remission of proteinuria in patients with nephrotic syndrome
- Reduces the rate of renal disease progression, delaying or avoiding need for dialysis or renal transplant
  - Strong heath/economic outcome
- Safety profile supported by development program and decades of use as excipient
- Convenient, subcutaneous delivery via patient-centric wearable device with wireless Bluetooth connectivity
  - Readily incorporated into combination therapy treatment algorithm without increasing the pill burden
- IP protection
  - 7 years orphan drug exclusivity in US, 10 years in EU
  - Exclusive worldwide license to IP related to 2HPβCD for treatment of kidney diseases
  - Expanded IP portfolio covering subcutaneous formulations/devices

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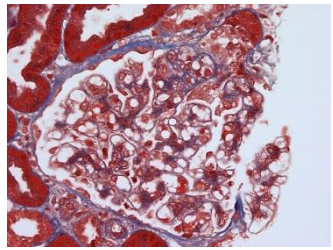
Role of Renal Lipid Accumulation in Kidney Disease

Excess Cholesterol in Podocytes Contributes to the Pathology of Glomerular Diseases

- The kidneys' filtration system, the nephron, includes a network of small capillaries known as the glomerulus
- Podocytes, which have long projections called foot processes, wrap around the capillaries; the space between them is known as a slit diaphragm (a lipid raft-like structure) serving as a selective barrier to prevent loss of protein in the urine (proteinuria)
- Maintenance of podocyte intracellular cholesterol at appropriate levels is critical to support the structural integrity and function of the podocytes and slit diaphragm; excess levels can compromise structural integrity

FSGS, Alport Syndrome, and Other Glomerular Diseases Are Associated With Excess Podocyte Cholesterol Resulting From Decreased Cholesterol Efflux



FSGS Patient's Podocyte Histology (Neptune)

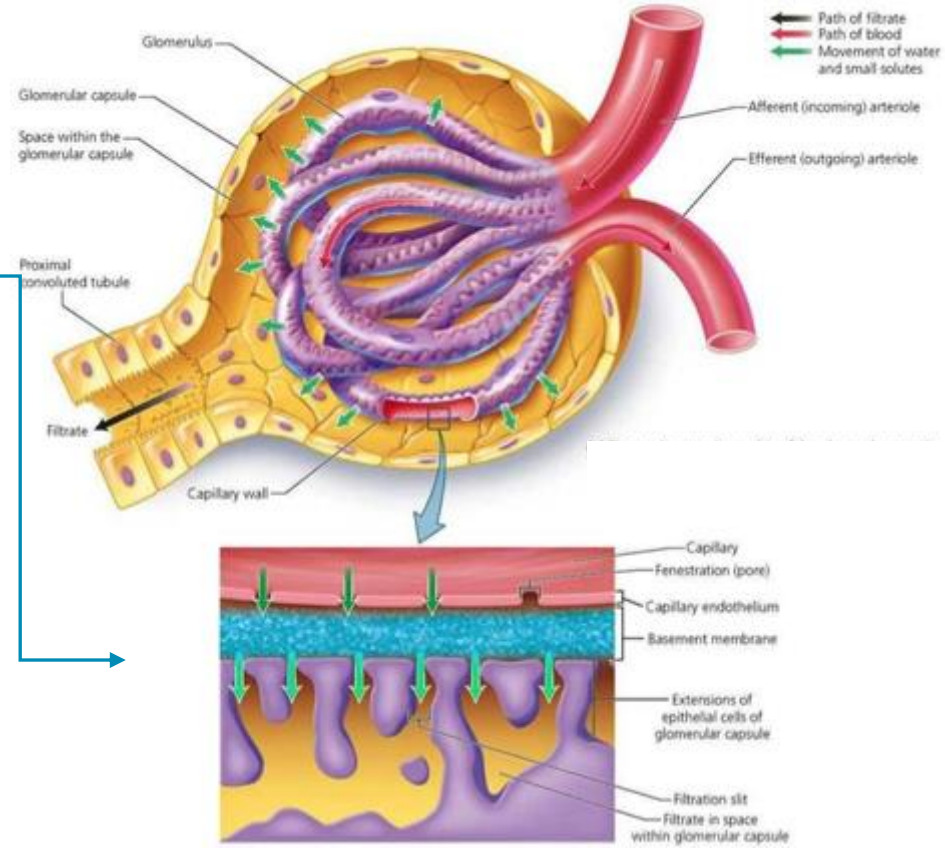


Image from: http://schoolbag.info/biology/humans/22.html

Fornoni A, Merscher S, Kopp JB. Lipid biology of the podocyte—new perspectives offer new opportunities. Nature reviews Nephrology. 2014;10(7):379-388. doi:10.1038/nrneph.2014.87.at

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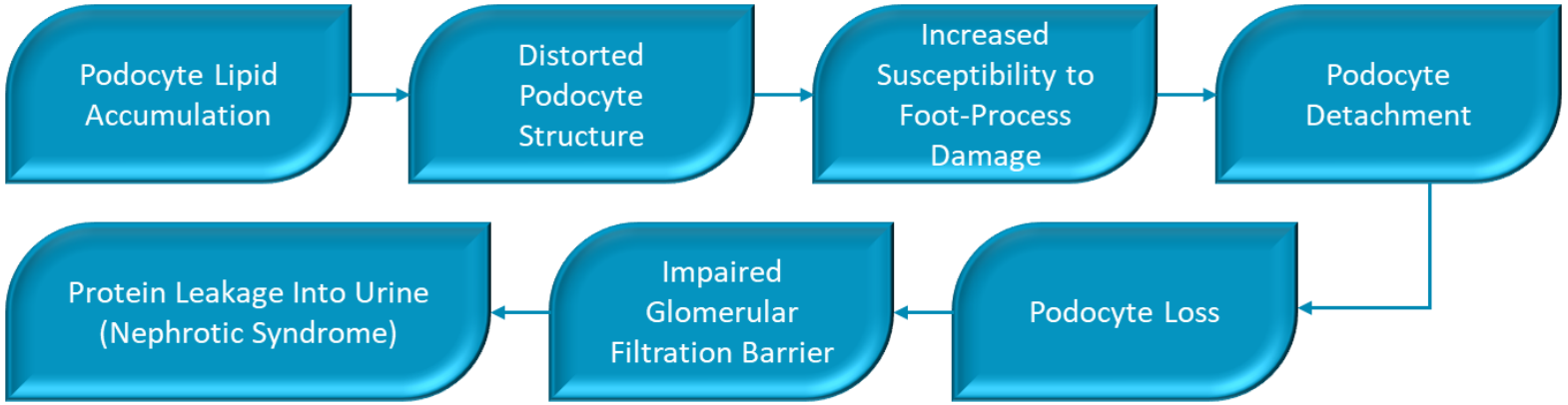
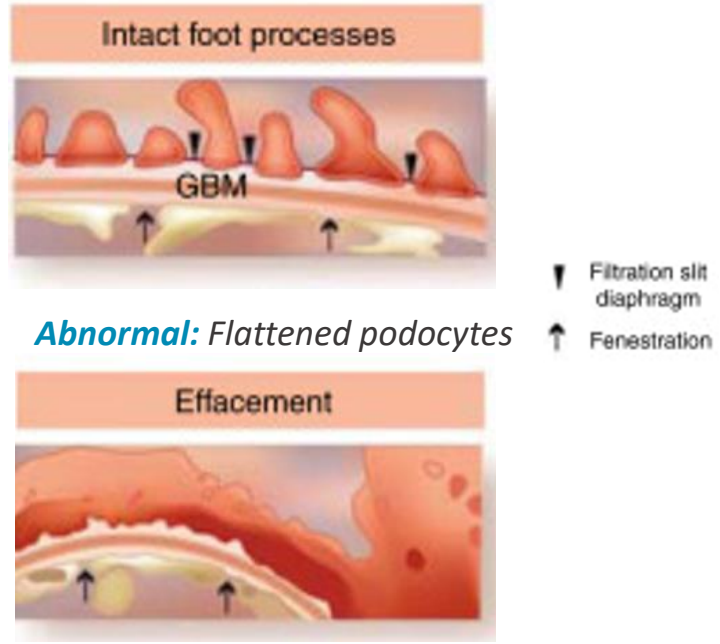
Accumulation of Glomerular Lipids Contributes to Structural Damage, Proteinuria, and Progression of Kidney Disease



Normal: *Intact podocyte foot process*



Abnormal: *Flattened podocytes*

Image Adapted From D'Agati VD:
Kidney Int. 2008 Feb;73(4):399-406

1. Ducasa GM, Mitrofanova A, Mallela SK, et al. ATP-binding cassette A1 deficiency causes cardiolipin-driven mitochondrial dysfunction in podocytes. J Clin Invest. 2019;129(8):3387–3400; D'Agati VD. Podocyte injury in focal segmental glomerulosclerosis: Lessons from animal models (a play in five acts). Kidney Int. 2008 Feb;73(4):399-406

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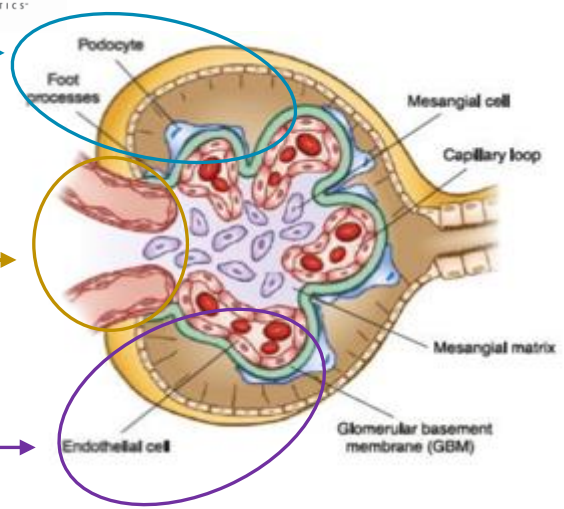
Current Treatment Algorithm For Nephrotic Syndrome Addresses Hypertension and Inflammation, But Not Lipids

- **Intracellular podocyte lipid accumulation from reduced cholesterol efflux** causes podocyte injury and flattened foot processes leading to proteinuria
  - No current treatments address podocyte lipid accumulation
- **Arteriole vasoconstriction** increases arteriole pressure leading to reduced blood flow and decreased glomerular filtration rate (GFR)
  - Treated with ACE inhibitors and ARBs to dilate the arterioles
- **Glomerular inflammation** results in distorted, more porous endothelial cells and contracted mesangial cells leading to proteinuria and decreased GFR
  - Treated with steroids and calcineurin inhibitors (CIs) to reduce or eliminate the inflammation

Chronic Kidney Disease



Healthy Kidney

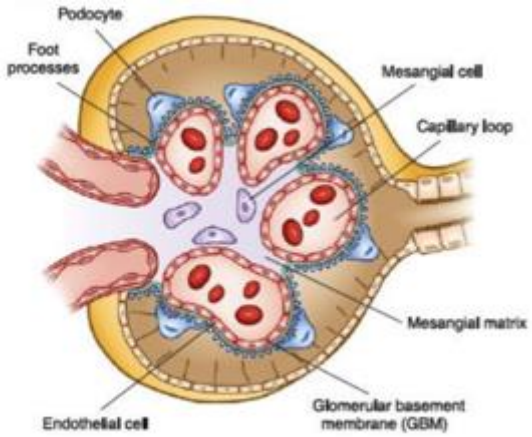
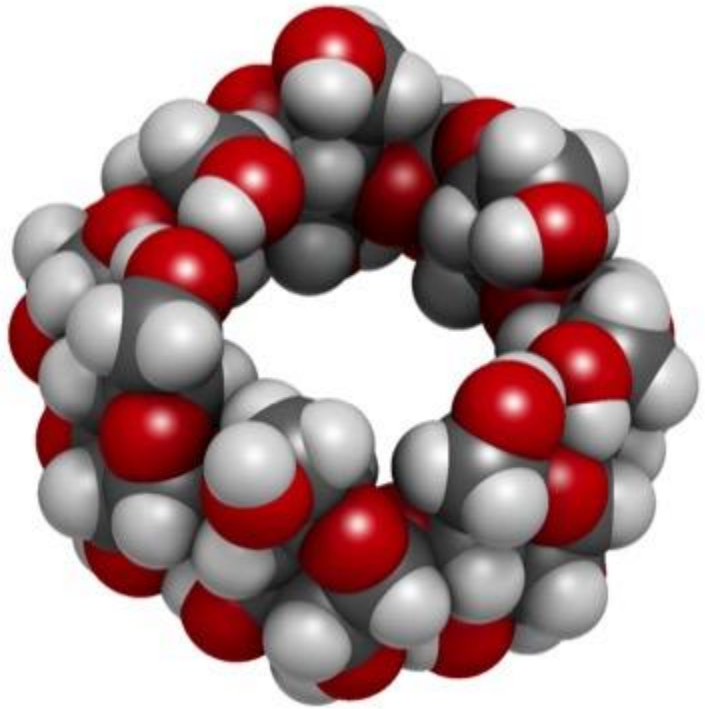


Image Adapted From Radica et al: Clin J Am Soc Nephrol 12: 2032–2045, 2017

No Drugs Target Glomerular Lipids

VAR 200, 2-Hydroxypropyl-Beta-Cyclodextrin (2HPβCD) Mediates Removal of Excess Cholesterol from Podocytes



Space filling model of
β-Cyclodextrin

Comprised of 7 Sugar Molecules Bound Together in a 3-D Ring

- 2HPβCD has a hydrophobic core that entraps and passively removes intracellular cholesterol from the kidney
- 2HPβCD is believed to mediate active cholesterol removal through upregulation of cholesterol efflux transporters ABCA1 and ABCG1
- Cholesterol removal restores renal structure and function

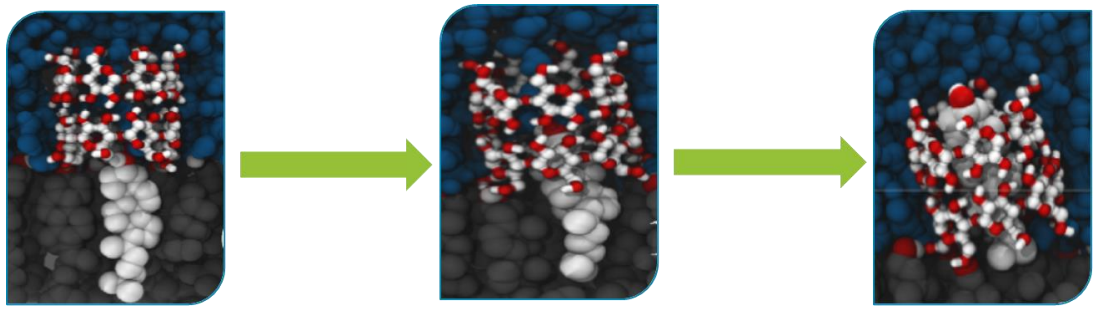


Image of βCD Adapted From Lopez et al: LoS Comput Biol 7(3): e1002020.
doi:10.1371/journal.pcbi.1002020

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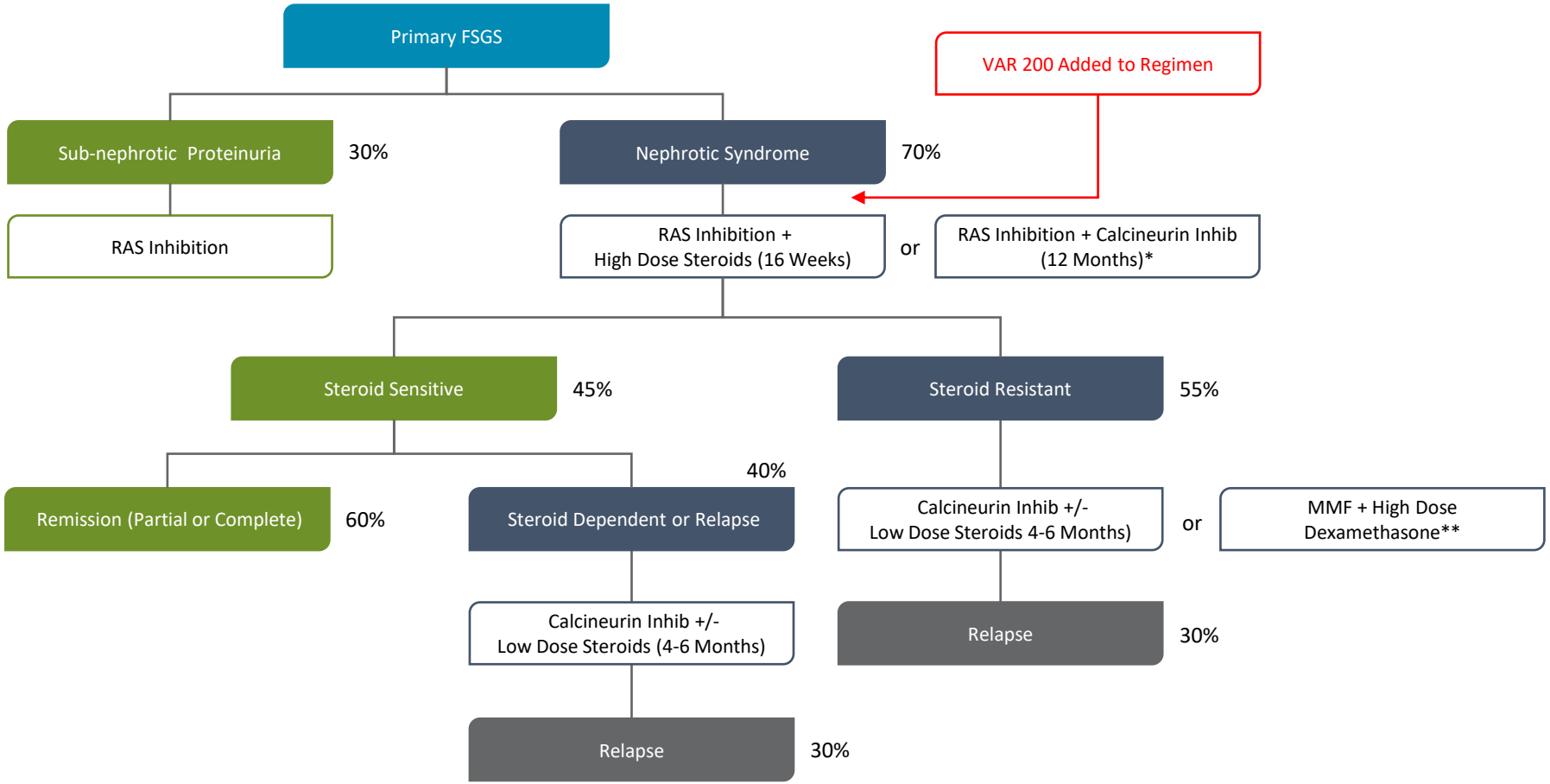
Current Treatment Algorithm Has Poor Response Rate, As Demonstrated in FSGS



*In patients with steroid intolerance or contraindication; **In patients who do not tolerate calcineurin inhibitors.

Beaudreuil S, et al: *Optimal management of primary focal segmental glomerulosclerosis in adults.* International Journal of Nephrology and Renovascular Disease 2017:10 97–107.

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Strong Pre-clinical Support for VAR 200, With POC in 3 Different Animal Models of Kidney Disease

Diabetic Kidney Disease Model

4,000 mg/kg 3x weekly

Compared to controls, VAR 200:

- Significantly reduced cholesterol levels in kidney cells
- Protected against kidney cell damage
- Reduced urinary protein starting 8 weeks
- Significantly reduced body weight and improved metabolic control (reduced blood sugar and serum insulin)

FSGS Models

40 mg/kg/day[1]; 4,000 mg/kg 3x weekly[2]

Compared to controls, VAR 200:

- Significantly reduced kidney cortex cholesterol
- Protected against kidney cell damage
- Reduced urinary protein (proteinuria) beginning at 8 weeks, with significant difference at 10 weeks

Reduction in proteinuria reproducible in two different models across three studies

1. Adriamycin induced; 2. Nfatc1^{nuc}

Alport Syndrome Model

4,000 mg/kg 3x weekly

Compared to controls, VAR 200:

- Significantly reduced cholesterol levels in kidney cells
- Significantly reduced kidney cell fibrosis and protected against damage
- Significantly reduced urinary and serum proteins starting at 3 weeks
- Normalized serum lipid profile

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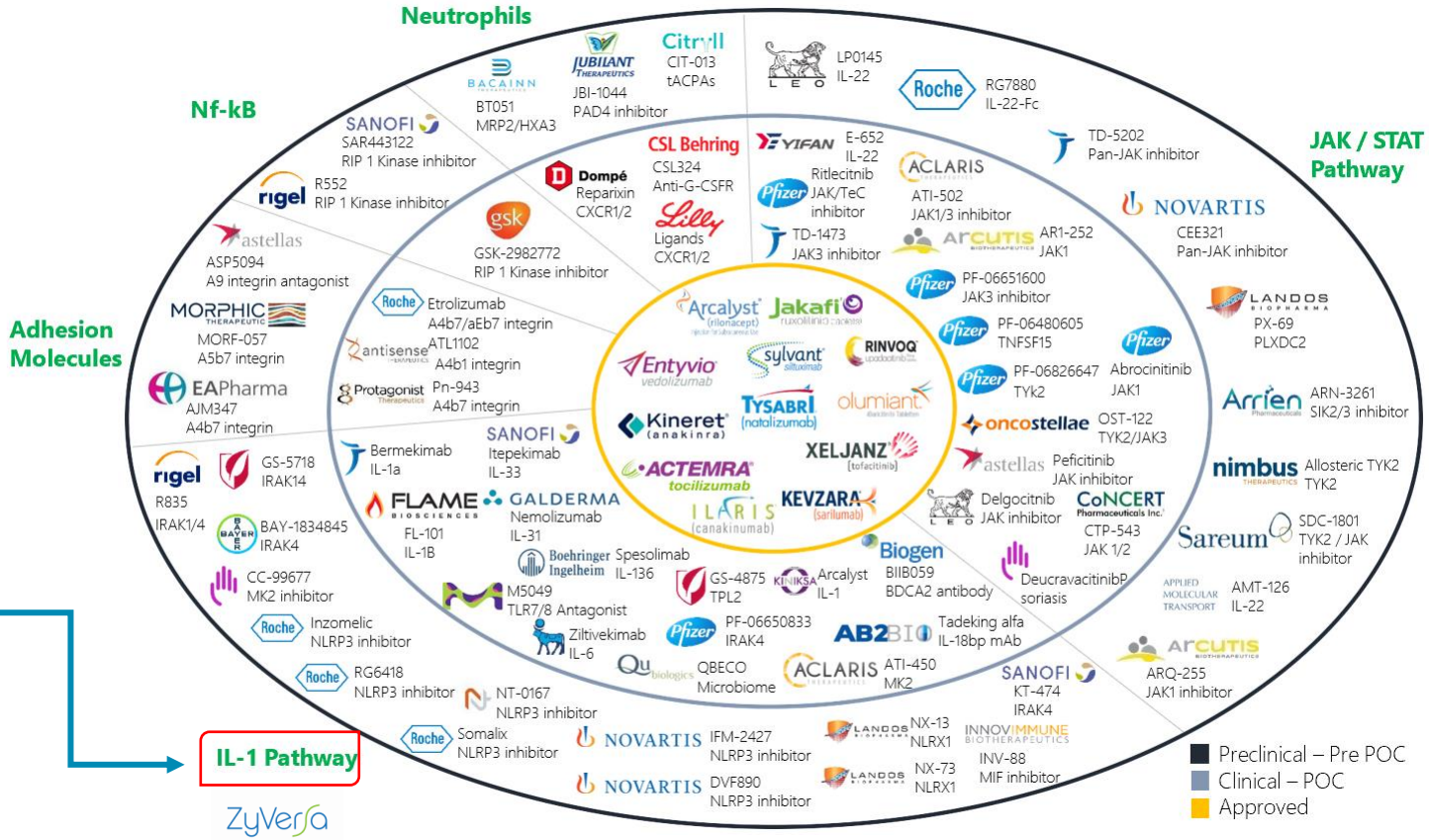
IC 100, Inflammasome Inhibitor Targeting ASC

Humanized Monoclonal IgG4 Antibody That Inhibits Initiation and Perpetuation of Inflammation Associated With >100 Inflammatory Conditions

Immune Therapies Have Significantly Evolved Over the Last 30 Years as Immune Response Mechanisms Have Become Better Delineated

Inflammasome Inhibitors Targeting IL-1 & IL-18 Cytokine Pathways Are Latest Generation

- Increased insight into B and T cell development, activation, and proliferation, cytokine and chemokine signaling, and complement activation has led to
  - More targeted therapeutics
  - Improved safety and efficacy
  - Opened opportunities for intervention in a broad range of diseases, both common and rare
- Inflammasome inhibitors target the innate immune system, blocking activation of IL-1β & IL-18, which promote immune responses and programmed cell death (pyroptosis) leading to exacerbation of inflammation



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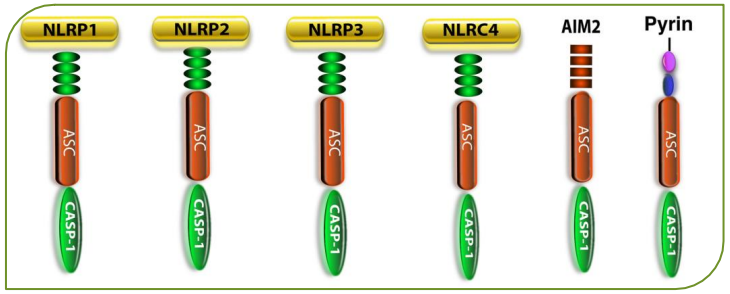
IC 100
ASC Inhibitor

Source: Torreya

IC 100 Uniquely Targets Multiple Inflammasome Sensors

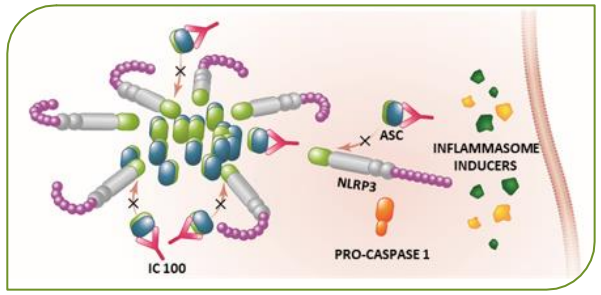
Designed To Maximize Control of Inflammation Across a Broad Range of Conditions Without Immunosuppression

Inhibits 12 or More Types of Inflammasomes To Control Inflammation Regardless of Its Triggers

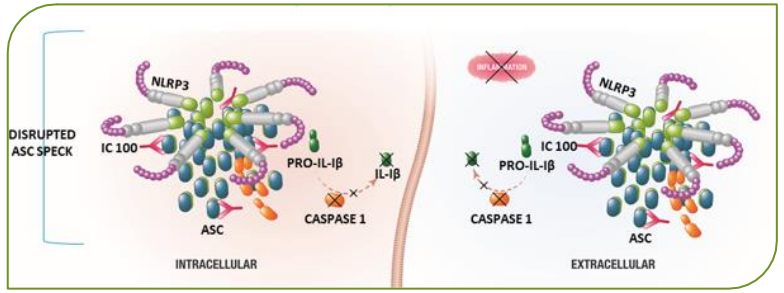


*Numerous conditions associated with activation of more than one type of inflammasome

Inhibits Inflammasome Formation To Block Initiation Of The Inflammatory Cascade



Disrupts ASC Speck Structure & Function To Block Perpetuation of Inflammation For Enhanced Control



NLRP3 Inhibitors Target Just 1 Type of Inflammasome, and Only Block Initiation of the Inflammatory Cascade

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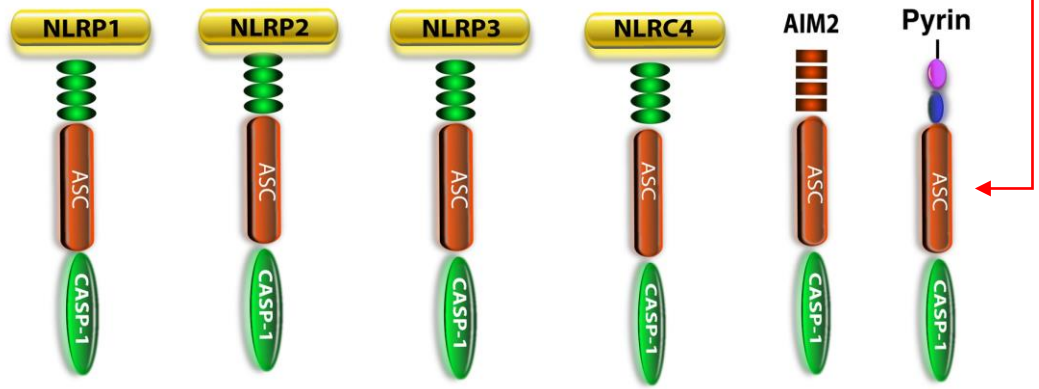
Inflammasomes Are the Central Signaling Hubs of the Innate Inflammatory Response

- Multiple inflammasomes are involved in innate immunity
- Inflammasomes are molecular complexes comprised of:
  - Sensor molecules including NLRP1, NLRP2, NLRP3, NLRC4, AIM2, and Pyrin (NLRP3 best known)
  - Adaptor protein ASC
  - Pro-caspase 1
- Each of the sensor molecules respond to different pathogens or danger signals
- ASC, which recruits pro-caspase 1 into the inflammasome, is involved with formation of 12 or more sensor molecules and their associated inflammasomes
- Caspase-1 activates the cytokine IL-1β to trigger an immune response
- Inflammasomes are named by their associated sensor molecule

Common Inflammasomes*

IC 100 Targets ASC Across Multiple Sensors



- NLRs (NOD-like receptor protein): Sense pathogens or endogenous sterile dangerous signals to activate the inflammasome
- AIM2 (Absent in melanoma 2): Senses bacterial and viral DNA to activate the inflammasome
- Pyrin: Senses bacterial toxins that modify RhoA GTPase to activate the inflammasome
- ASC (Apoptosis associated speck-like protein containing a caspase activating recruitment domain): Mediates the interaction between the NLR sensor and pro-caspase 1 in the inflammasome complex
- Caspase 1: Activates the cytokine IL-1β to trigger inflammation

*ASC also serves as an adaptor protein in the formation of the following inflammasomes: NLRP6, NLRP7, NLRC5, NAIP2, NAIP5, NAIP6

1. Guo H, Callaway JB, Ting JP. Inflammasomes: mechanism of action, role in disease, and therapeutics. Nat Med. 2015;21(7):677-87; 2. Agrawal I, Jha S. Comprehensive review of ASC structure and function in immune homeostasis and disease. Mol Biol Rep. 2020 Apr;47(4):3077-3096

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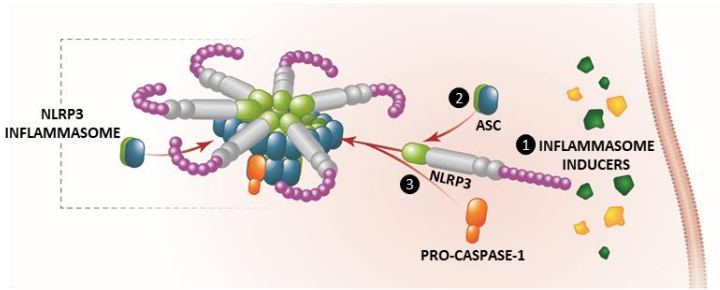
ASC Plays a Critical Role in Initiation, Amplification, and Perpetuation of the Inflammatory Response

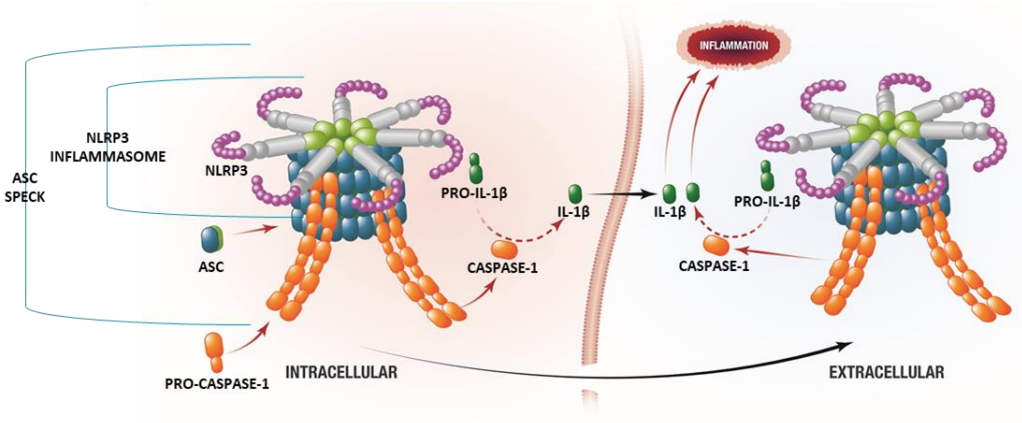
IC 100 Inhibits ASC, Blocking Initiation & Perpetuation of Inflammation

- Activated inflammasomes serve as a docking platform for additional ASC molecules which polymerizes in a prion-like structure to form a large filamentous signaling platform, known as an ASC Speck
- ASC Specks provide a scaffold for pro-caspase-1, triggering its activation and maturation IL-1β, initiating the inflammatory process
- Caspase-1 drives cleavage of Gasdermin D, which triggers pyroptosis, releasing active cytokines and ASC specks into the extracellular space
- Activation and release of IL-1β continues, heightening and perpetuating the inflammatory response in neighboring cells and tissues

Inflammasome Formation



ASC Speck



1. Guo H, Callaway JB, Ting JP. Inflammasomes: mechanism of action, role in disease, and therapeutics. Nat Med. 2015;21(7):677-87; 2. Franklin BS, Bossaller L, De Nardo D, et al. The adaptor ASC has extracellular and 'prionoid' activities that propagate inflammation. Nat Immunol. 2014;15(8):727-37; 3. Shaw PJ, McDermott MF, Kanneganti TD. Inflammasomes and autoimmunity. Trends Mol Med. 2010;17(2):57-64

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ASC, Inhibited by IC 100, is a Component of at Least 12 Types of Inflammasomes;
Numerous Inflammatory Disorders Associated with Activation of Multiple Types of Inflammasomes

Inflammasomes and Disease

Dysregulated inflammasome activation is involved in a myriad of diseases and conditions:

- **Autoimmune Diseases:** Multiple sclerosis, systemic lupus erythematosus, lupus nephritis, rheumatoid arthritis and colitis
- **Metabolic Diseases:** Diabetes, atherosclerosis, non-alcoholic fatty liver disease and gout
- **Neurodegenerative Diseases:** Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis
- **Secondary Injury:** Spinal cord injury, traumatic brain injury and stroke
- **Cancer:** Lung cancer and melanoma

Disease/Condition	Inflammasomes Implicated	References
Multiple Sclerosis	AIM2, NLRP1, NLRP2, NLRP3, NLRC4	Huang 2004; Soulika 2009; Maver 2017; Freeman 2017; Noroozi 2017; Soares JL 2019
Lupus Nephritis	AIM2, NLRP3	Choubey and Panchanathan 2017; Cytokine 2019; Fu 2019
Diabetic Nephropathy	AIM2, NLRP3	Anders and Muruvue 2011; Hutton 2016
CNS Injury	AIM2, NLRP1, NLRP2, NLRP3	de Rivero Vaccari 2008, 2009, 2012; Abulafia 2009; Liu 2013; Bartolotti 2018
Alzheimer's Disease	AIM2, NLRP1, NLRP3	Ahmed 2017; Venegas 2017; White 2017; Wu 2017; Lang 2018
Rheumatoid Arthritis	AIM2, NLRP1, NLRP3, NLRP6	Goh 2017; Grandemange 2017; Li 2018; Addobbatti 2018; Lin and Luo 2016; Sode 2015; Wang 2014
Inflammatory Bowel Disease	AIM2, NLRP1, NLRP3, NLRP6, NLRC4	Vanhove 2015; Ratsimandresey 2017; Lazaridis 2017; Kanneganti 2017; Normand 2011; Levy 2015; Seregin 2017; Tye 2018; Williams 2018; Opipari and Franchi, 2015

ASC Inhibition Expected to Effectively Control Inflammation In Diverse Indications

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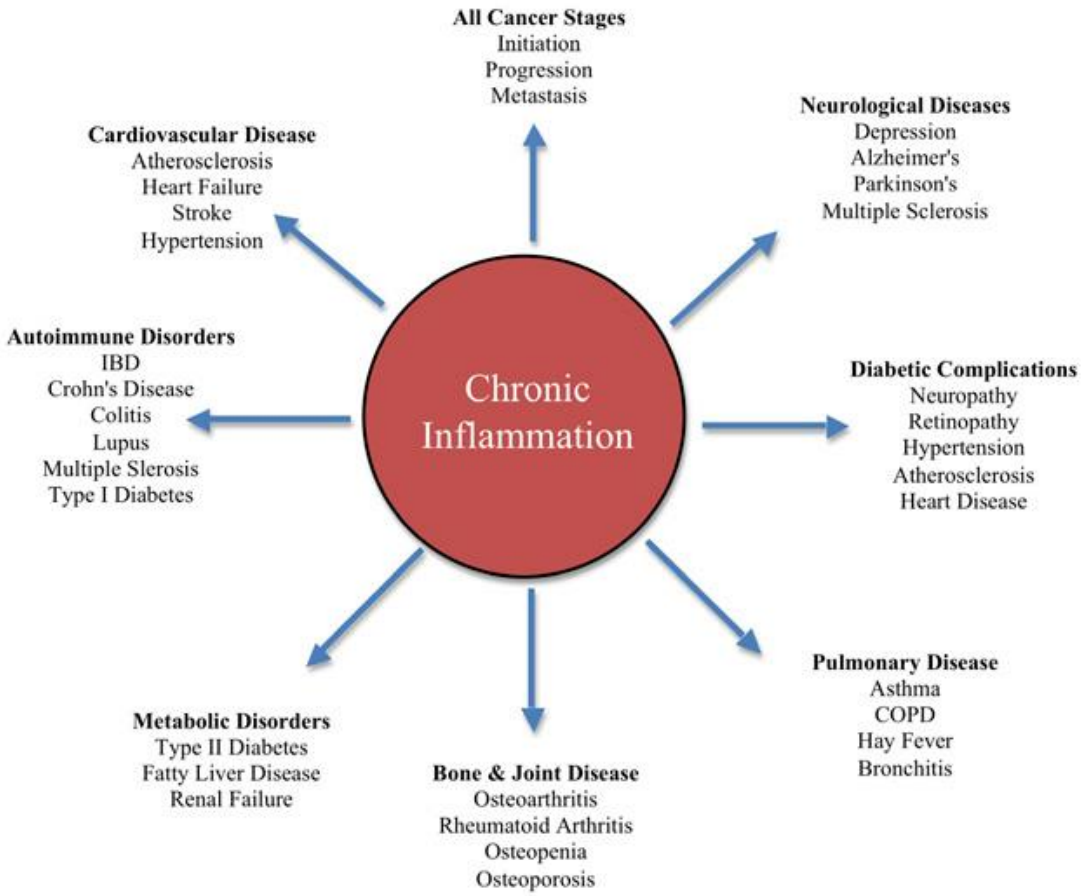
IC 100, a Pipeline Within a Product



IC 100 Has Potential in Both CNS and Non-CNS Diseases

CNS Conditions:

- Penetrates brain and spinal cord
- Promising preclinical data in MS (IND-ready), spinal cord and traumatic brain injury (mechanistic proof-of-concept)

Non-CNS Conditions:

- Promising preclinical data in ARDS (IND-ready)
- Strong scientific rationale and pharmacologic signal in type II diabetic nephropathy

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Preclinical Roadmap - Indication Expansion Strategy

Current IND-Ready Indications	Wave 2 Preclinical Assessments	Wave 3 Preclinical Assessments
Acute Respiratory Distress	IgA Nephropathy	Huntington's Disease
Multiple Sclerosis	Pancreatic Cancer	Congestive Heart Failure
	Parkinson's Disease	Early Cognitive Impairment

Orphan Indications
Non-orphan Indications

Scientific/Medical Criteria

- Multiple inflammasome associated with pathogenesis
- Cytokines drive pathogenesis &/or progression
- Inhibition of inflammasomes positively impact outcomes
- Unmet Medical Needs
- Availability of Accepted Animal Models
- Established Clinical Endpoints

Commercial Criteria

- Market size (orphan or large market)
- Competitive landscape
- Payor perceptions

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IC 100 Proof-of-Concept

Multiple Sclerosis, Acute Respiratory Distress Syndrome

IC 100 Preclinical Results

IC 100 Preclinical Results
Proof of Concept
• MS has potential as a lead indication (POC established in EAE model of MS)
• ARDS has potential as a secondary indication (POC established in ALI model of ARDS)
• Mechanistic POC established in animal models of spinal cord injury and traumatic brain injury
Safety
• MS animal study has shown attenuation of inflammation without immunosuppression
• Epigenetic screening has shown lower immunogenicity than many biologics
• Initial toxicology studies in rodents and NHP showed no significant safety issues, with a NOEL of 300mg/kg
Characterization
• Long projected half-life: 24 days*
• Strong binding affinity across human/non-human primate, mouse, and rat (KD < 1 nM), with fast association rates and low dissociation rates
• In vivo bioluminescence imaging showed that IC 100 has broad tissue distribution, crosses the blood brain barrier, and readily penetrates brain and spinal cord
• In naïve mice, liver, lung, kidney, heart, ovary and thyroid tissues were major sites of IC 100 penetration
• Confocal microscopy of fluorescently-labeled IC 100 revealed IC 100 is rapidly taken up by CNS cells and by a variety of immune cell populations
• Cell-free inflammasome assays and whole human blood inflammasome assays demonstrated that IC 100 acts intracellularly and extracellularly
• IC 100 inhibited intracellular inflammasome activation evidenced by reduction of caspase-1 processing, and it inhibited ASC oligomerization resulting in decreased release of IL-1β

* Consistent with IgG4 half-life of 21 – 24 days[1]; Based on single dose half-life study in mice (half-life 8 – 14 days)

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IC 100 Has Preclinical Data Substantiating Its MOA in Multiple Indications

Multiple Sclerosis (MS)

- MS is characterized by an inflammatory response dependent on lymphocyte and myeloid cell activation
- IC 100 resulted in a lower number of activated myeloid and microglial cells, and improved clinical outcomes consistent with these changes

Spinal Cord Injury (SCI)

- Following SCI, expression of NLRP1 inflammasome signaling molecules, including ASC, are increased and NLRP1 inflammasome is activated in spinal cord neurons, triggering an inflammatory response
- ASC inhibition decreased inflammasome activation, reduced spinal lesions, and improved behavioral outcomes

Inflammaging (Age-related Inflammation)

- Inflammasome signaling proteins, NLRP1, ASC, caspase-1, caspase-8, and IL-1β are significantly increased in the cortex of aged mice
- IC 100 inhibits NLRP1 inflammasome activation that occurs in aged mice
- IC 100 significantly reduced ASC Specks, IL-1β, and inflammasome protein expression (NLRP1, ASC, caspase-1, and caspase-8)

Penetrating Ballistic-Like Brain Injury Model (PBBI)

- Following PBBI, expression of inflammasome signaling molecules, including ASC, are increased, and inflammasomes are activated triggering an inflammatory response and pyroptosis
- IC 100 decreased inflammasome activation and pyroptosis when compared with vehicle control

Fluid Percussion Brain Injury Model (FPI)

- Following FPI, expression of inflammasome signaling molecules, including ASC, are increased and inflammasomes are activated in cerebral cortex neurons, triggering an inflammatory response
- ASC neutralization reduced inflammasome activation and decreased brain contusion volume associated with inflammation when compared with control

Acute Respiratory Distress Syndrome (ARDS)

- Inflammasome activation and inflammation play a central role in lung injury in ARDS
- IC 100 inhibited inflammasome activation and improved histopathological outcomes in lung tissue

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Intellectual Property

Intellectual Property

VAR 200

- Exclusive, worldwide license to 2HPβCD IP for the treatment of kidney disease in humans
  - Portfolio of issued and pending patents in the US and other countries
  - Two patent families covering
    - Glomerular disorders and disease
    - Diabetic Kidney Disease
- Anticipated orphan drug exclusivity for FSGS and Alport Syndrome
  - 7 years market exclusivity in US; 10 years in EU
- IP strategy includes plans to file for new formulations in development, dosing regimens, and administration routes

IC 100

- Exclusive, worldwide license to therapeutic and diagnostic use of inflammasome-targeted inventions in all indications
  - Portfolio of issued and pending patents in the US and other countries
  - Five patent families covering
    - Composition of Matter
    - Biomarkers
    - Methods of use
- IP strategy directed to broad protection of IC 100 as a platform for inflammatory conditions, including treatment and diagnosis of our pipeline indications, and a wide spectrum of other autoimmune, neurodegenerative, and metabolic diseases, or trauma
- Actively filing formulations in development, dosing regimens, administration routes, and new indications

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Inflammasome-Opportunity: >$4B M&A Activity by Roche, Novartis and BMS Last 18 Months[1]

Renal & Anti-inflammatory Programs Targeting $75B TAM[2] [3]

VAR 200: Novel Cholesterol Efflux Mediator with Orphan Renal Focus

IC 100: Differentiated mAb Inflammasome ASC Inhibitor; Potential for Broad Range of Indications

Proven Leadership in Drug Development, M&A, Financing; Renowned SAB in Renal and Immunology

1. Pitchbook as of 12/2/20
2. Chronic Kidney Disease Drugs Market Analysis. Coherent Market Insights, November 2020
3. Anti-Inflammatory Biologics Market Size, Share & Industry Analysis. Fortune Business Insights, May 2020

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