HEPION PHARMACEUTICALS

Our AI-Driven Bioinformatics Platform is Expected to Accelerate the Development of a Novel NASH Therapeutic and Create Pathways to Optimize Efficacy

Nasdaq LISTED HEPA

Filed pursuant to Rule 433 of the Securities Act of 1933
Issuer Free Writing Prospectus dated November 18, 2020
Relating to the Preliminary Prospectus dated November 18, 2020
Registration Statement File No. 333-249724

Forward-Looking Statements

This presentation may contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Such forward-looking statements are characterized by future or conditional verbs such as “may,” “will,” “expect,” “intend,” “anticipate,” “believe,” “estimate” and “continue” or similar words. You should read statements that contain these words carefully because they discuss future expectations and plans, which contain projections of future results of operations or financial condition or state other forward-looking information. Such statements are only predictions and our actual results may differ materially from those anticipated in these forward-looking statements.

We believe that it is important to communicate future expectations to investors. However, there may be events in the future that we are not able to accurately predict or control. Factors that may cause such differences include, but are not limited to, those discussed under Risk Factors in our periodic reports and our Registration Statement filed with the Securities and Exchange Commission, including the uncertainties associated with product development, the risk that products that appeared promising in early clinical trials do not demonstrate safety and efficacy in larger-scale clinical trials, the risk that AI-POWR™ fails to help us discover and develop product candidates, the risk that we will not obtain approval to market our products, risks associated with delays, increased costs and funding shortages caused by the COVID-19 pandemic; the risks associated with dependence upon key personnel and the need for additional financing. We do not assume any obligation to update forward-looking statements as circumstances change.

Free Writing Prospectus

Hepion Pharmaceuticals, Inc. has filed a registration statement (including a preliminary prospectus) (the “Registration Statement”) with the Securities and Exchange Commission (the “SEC”) on Form S-1 (SEC File No. 333-249724) for the offering to which this prospectus relates. This presentation highlights basic information about us and the proposed offering. Because it is a summary, it does not contain all of the information that you should consider before investing. The registration statement has not yet become effective. Before you invest, you should read the prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and the offering.

You may access these documents for free by visiting EDGAR on the SEC Web site at http://www.sec.gov. Alternatively, we or any underwriter participating in the offering will arrange to send you the prospectus if you contact ThinkEquity, a division of Fordham Financial Management, Inc., Prospectus Department, 17 State Street, 22nd Floor, New York, New York 10004, telephone: (877) 436-3673 or email: prospectus@think-equity.com.

This presentation does not constitute an offer or invitation for the sale or purchase of securities or to engage in any other transaction with Hepion Pharmaceuticals or its affiliates. The information in this presentation is not targeted at the residents of any particular country or jurisdiction and is not intended for distribution to, or use by, any person in any jurisdiction or country where such distribution or use would be contrary to local law or regulation.

The cost to develop one New Drug is $2.6 Billion: the approval rate for Drugs Entering clinical development is less than 12%

Tufts Center for the Study of Drug Development, 2019

Intercept

FDA Rejects NASH Therapeutic, June 2020

GENFIT
TOWARDS BETTER MEDICINE

Fails Phase 3 Trial, May 2020

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ROBERT FOSTER, PharmD, PhD
President, CEO Hepion Pharmaceuticals, Inc.

AI-driven bioinformatics has the potential to transform healthcare

The net-net for biotechs like us is to create the ability to mitigate risk, shorten timelines, and reduce the costs of our trials while creating additional value for our platform.

HIGHLIGHTS

- Clinical phase 2a NASH program currently underway
- Anticipated that Artificial Intelligence and Smart Algorithms Platform (**AI-POWR™**) will help to identify and optimize responder outcomes
- Strong safety/tolerability profile in preclinical and phase 1 clinical studies (n=73 healthy volunteers)
- Strong preclinical proof of concept in fibrosis and viral infections
- Orally active, once daily capsules
- Regulating protein folding cyclophilins (enzymes) to treat diseases including:
  - Fibrosis, viral infections, cancers, etc.
- 30 years experience in this very specific field of chemistry and drug development
  - Core team that founded Aurinia Pharmaceuticals (NASDAQ:AUPH), and discovered and developed voclosporin through Phase 2
- Robust IP (protection in major markets including US, Europe, Australia, Canada, China, Japan, Korea) with exclusivity until 2039 with potential further regulatory exclusivity up to 2044

TWO VALUE DRIVERS

HEPION PHARMACEUTICALS CRV431

A Therapy for NASH with indications for several other conditions

HEPION PHARMACEUTICALS AI-POWR™

AI-Driven, Bioinformatic Platform

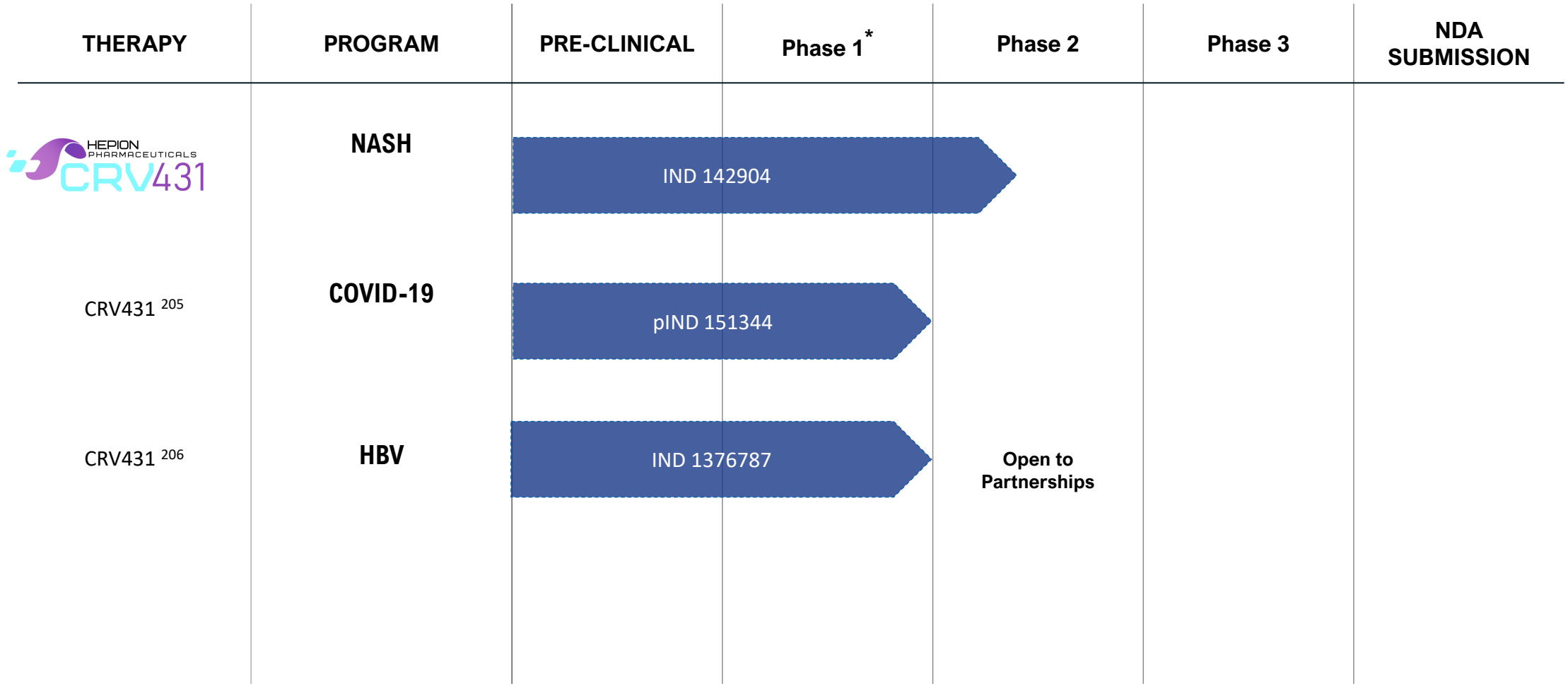
CASH

$13.7 M as of 9/30/20

COVERAGE

Elemer Piros, Ph.D. – Roth Capital
Kumar Raja, Ph.D. – Brookline Capital
Nathaniel Calloway, Ph.D. – Edison Group

PIPELINE



*Separate Phase 1 programs were not conducted for each separate indication. The Phase 1 program was comprised of Single and Multiple Ascending Doses, and a Drug-Drug Interaction study.

ABOUT US

We Have Developed an AI-Driven Bioinformatics Platform Which is Expected to Accelerate Cost-Effective Clinical Trials Study Design to Increase Response Rates

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AI-POWR™

Bioinformatics ACCELERATES the Development of Our OWN THERAPIES and can be used as a PLATFORM

A I	P	O	W	R
Supervised and unsupervised AI-enabled machine learning	Precision medicine based on genetics, environment, and lifestyle	Omics, including genomics, proteomics, metabolomics and lipidomics	World, accessing world genomic databases	Response and clinical outcomes

AI-POWR™

Hepion's AI-POWR™ platform provides integrative, multi-variate, systems-biology bioinformatic and big-data analysis of proprietary pre-clinical and clinical data with publicly-available multi-omic data bases and key clinical outcomes. Analytics provide for drug target selection, clinical study design enhancement and *a priori*-responder analysis. We believe that the AI outputs will provide us with the following benefits:

- Novel Drug Target Selection (for pipeline drugs)
- Biomarker Selection and Validation
- Patient Selection (*a priori*-responder analysis)
- De-Risk Clinical Trials
- Improve drug development efficiency with cost savings

Identifying Responders Increases "Signal-to-Noise"

Identify Responders from Big Data Sources
using multi-omic approach (genomics, proteomics, metabolomics, lipidomics, patient traits)

AI-POWR™

Supervised and Unsupervised Machine Learning Algorithms
Model Inputs and Run Scenarios to Constantly Increase Response Rates

AI-POWR™ Expected to Produce a Concentrated Set of Responders Which we Believe Will:

- Help to identify responders *a priori*
- Reduce need for *post-hoc* analysis
- Optimize spread between treatment and placebo

Components AI-POWR™

ACCESSING DATA Inputs
Are All Publicly Available, for everyone

Big Data Access
We all have access to millions of studies, results and findings are now compiled for:

- ✓ Disease State Specific Genomic
- ✓ Proteomics, Genomics, Lipidomics, Metabolomics ('Multi-Omics') Data Bases
- ✓ Patient Traits
- ✓ Clinical Outcomes

Data Mining

AI DATA-PROCESSING
Is the Tough, and Proprietary part

Scripting Algorithms / AI
Developing Big Data Processing Algorithms
Supporting Predictions and Actions

Continuous Learning

Fine Tuning
Algorithm Adjustment of
Datasets / New Biomarkers
Patient Selection
Study Design Enrichment

DEFENDING OUTCOMES
Are the Ultimate Goals of Bioinformatic AI Platforms.

Demonstrate Improved Response Outcomes Through:
Patient Selection
Biomarker Selection
Drug Target Selection

Collect and Prepare Assessments for Trial Study Submission
Clinical Success
De-Risk Failure
Improve Study Efficiencies
Cost Savings
Re-Analysis-Feedback

THE NET BENEFITS of AI-Driven, Bioinformatic Trials and Study Design

Anticipated Benefits of AI-Enabled Bioinformatics in Trials and Study Design

Increase Trial Success Rates
Phase I-III selection and biomarker verification reduce variability and increase study power which results in high levels of efficacy in clinical trial phases

Shorten Trial Timelines
Modeling results, adjusting variables and honing scenario-based study designs shorten review times

Decrease Costs
Shortening intervals between trials and decreasing the amount of time and effort and cost required to resubmit studies during trials

Novartis used AI to predict and monitor trial costs, enrollment and quality. As a result, the company reported a 10-15 % reduction in patient enrollment times in pilot trials. Healthcare Weekly, 2019.

The Pain Points in Traditional Clinical Trials Today – Long timelines, high costs and low response rates

PHASE 1	PHASE 2	PHASE 3
Takes at least 3-6 months. Around 70% move to next phase	**Takes 1-2 years. Around 33% move to next phase.**	**Takes 1-4 years. Around 25-30% move to next phase.**

Traditionally, most time and money are spent for trials which have the lowest efficacy rates. Patient targeting and recruitment accounts for approximately 32% of costs. Deloitte, 2019


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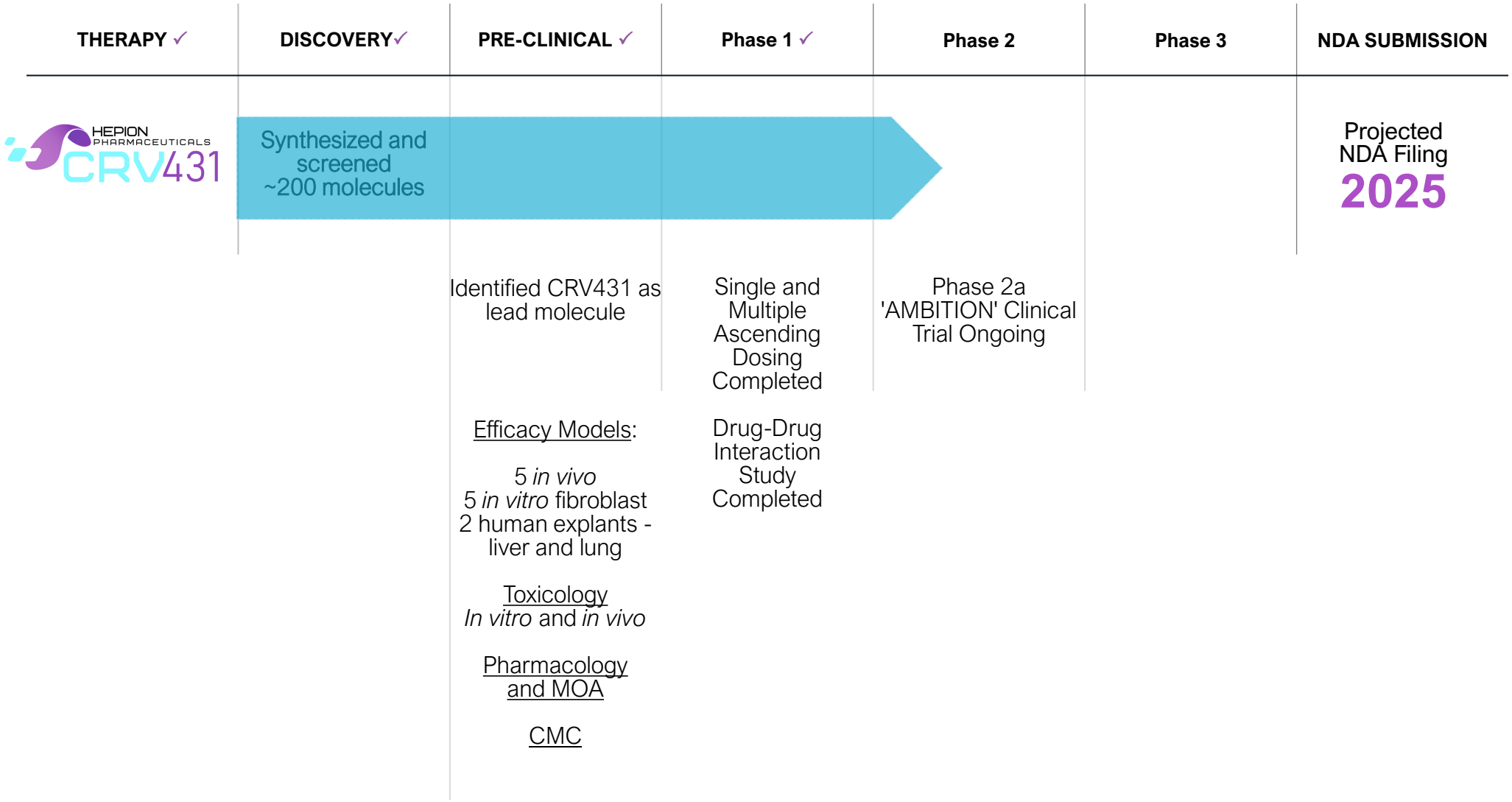
CRV431
a cyclophilin inhibitor in development
using AI-POWR™ to produce anticipated
market-leading efficacy rates to treat
NASH

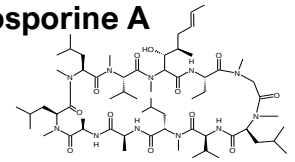
CRV431 for NASH



THE GENESIS OF CRV431

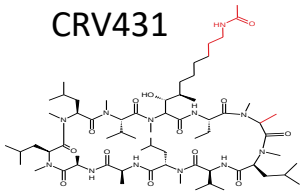
Theory	Prediction and Experimentation	Findings
Modifying Cyclosporine A can greatly increase its immunosuppressive benefits	Modifications of Cyclosporine A can either eliminate or enhance immunosuppression. Our team's past discovery, voclosporin, was chemically modified to enhance immunosuppression	Inhibition of each cyclophilin isoform produces distinct therapeutic effects

Cyclosporine A



Nearly 40 years of clinical use as immunosuppressive drug for organ transplantation and autoimmune diseases

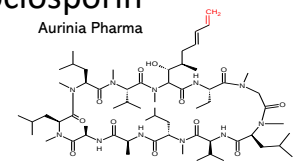
CRV431



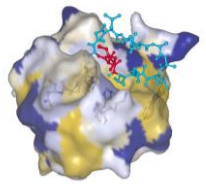
Modifications increase affinity for cyclophilins (13-fold) and **eliminate immunosuppression**

Voclosporin

Aurinia Pharma



Modifications increase affinity for calcineurin and **increase immunosuppression potency**



CRV431 binds potently (Ki≈1 nM) to around 10 of 17 cyclophilin isoforms in the human body

WHY TARGET CYCLOPHILINS

Cyclophilins shown to play negative roles in:

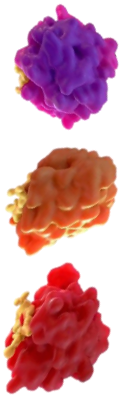
Viral Hepatitis • Cancers • Acute And Chronic Lung Injury • Myocardial Infarction • Stroke • Arthritis • Atherosclerosis • Thrombosis • Aortic Aneurysm • Coronary Artery Disease • Pulmonary Arterial Hypertension • ALS • Alzheimers Disease • Multiple Sclerosis • Muscular Dystrophies • Traumatic CNS Injury

Patent Portfolio

Family 1	Composition of Matter 47 Issued Patents 
Family 2	CRV431 Formulation International PCT Application US Patent Application Nov 2019
Family 3	Treatment of Fibrotic Disease in Multiple Organs US Provisional Patent Application Feb 2020
Family 4	Anti-Fibrotic and Anti-Cancer Activities US Provisional Patent Application Feb 2020
Family 5	AI-POWR: Biological Study Design and Results Analysis US Provisional Patent Application July 2020 US Trademark Application July 2020
Family 6	CRV431 and COVID-19 US Provisional Patent Application Oct 2020

CRV431 MODE OF ACTION

Cyclophilin enzymes regulate the structure and activity of many proteins throughout the body

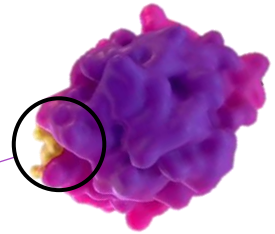


Regulatory roles of cyclophilins in many disease pathways make them good candidates as drug targets

CRV431

Pan-Cyclophilin Inhibitor

Binds to Cyclophilin A to reduce inflammation

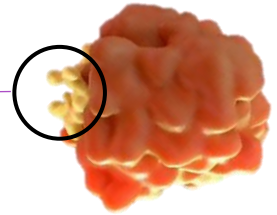


Cyclophilin A (cytosol and secreted)

Secreted from injured cells and acts as proinflammatory cytokine by binding to CD147.

- Hijacked by viruses to assist in viral replication (e.g. SARS-CoV-2)

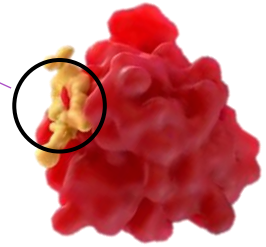
Binds to Cyclophilin B to reduce fibrosis



Cyclophilin B (endoplasmic reticulum)

Promotes fibrotic scarring by controlling collagen production

Binds to Cyclophilin D to mitigate mitochondrial damage



Cyclophilin D (mitochondria)

Promotes mitochondrial pore opening leading to mitochondrial and necrotic cell death

Regulates mitochondrial metabolism

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AI-POWR™

CRV431

The Development of
CRV431 Using AI-POWR™

Preclinical Antifibrotic Efficacy

FIBROSIS – a response to chronic injury – is a major cause of organ dysfunction and its reduction is the primary goal in the treatment of NASH

Human Cell Cultures		CRV431 Effects
Hepatic stellate cells, fibroblasts (multiple organs)	TGFβ or endogenous stimulation	▼fibrotic gene expression ▼ procollagen and fibronectin secretion

Human Tissue Explants	(Precision Cut Slice Cultures)	CRV431 Effects
Liver explants (4 donors)	TGFβ+PDGF-BB or endogenous stimulation	▼ inflammatory/fibrotic gene expression ▼ inflammatory/fibrotic protein secretion
IPF lung explants (1 donor)	Endogenous stimulation	▼ tissue fibrosis

Animal Models (8 independent studies)		CRV431 Effects
Mice (liver fibrosis)	Western diet + carbon tetrachloride	82%▼ fibrosis; ▼ weight gain
Mice (liver fibrosis)	High fat diet + streptozotocin (4 studies)	37-57%▼fibrosis; ▼ weight gain;50%▼liver tumors
Mice (liver fibrosis)	Carbon tetrachloride	44%▼ fibrosis
Mice (kidney fibrosis)	Unilateral ureter obstruction	42%▼ fibrosis
Rats (liver fibrosis)	Thioacetamide	48%▼ fibrosis; prevented cirrhosis

PHASE 1 STUDIES – Safety, tolerability and pharmacokinetics (PK)

CRV431 in Healthy Subjects

Single Ascending Dose (SAD)	Multiple Ascending Dose (MAD)	Drug-Drug Interaction (DDI)
✓ N = 32 (24 CRV431; 8 Placebo). ✓ Doses: 75 mg, 225 mg, 375mg, 525 mg (single doses) ✓ Drug Exposure is in the range in which efficacy was demonstrated in pre-clinical models. ✓ Pharmacokinetics are first order and support once daily dosing. ✓ No SAE's, Mild AE's, No dose response in AE's or changes in clinical labs. ✓ No changes in vital signs or ECG.	✓ N = 25 (All CRV431). ✓ Doses: 75 mg, 150 mg, 225 mg, 300 mg, 375 mg QD x 28 Days. ✓ Drug Exposure starting at 75 mg QD is in the range in which efficacy was demonstrated in pre-clinical models. ✓ Pharmacokinetics are first order and support once daily dosing. ✓ No SAE's, Mild AE's, No dose response in AE's or changes in clinical labs. ✓ No changes in vital signs or ECG. ✓ Data supported initiation of Phase 2a NASH Trial	✓ N= 18 ✓ Single CRV431 Drug Interaction Study with tenofovir

Example of AI-POWR™ Utility with CRV431 in NASH/NAFLD Liver Slices

AI-POWR™ Rapid and Early Identification of Key NASH-Related Genes Altered by 3-Days CRV431

- NASH/NAFLD is heterogenous
- Genetic analysis of the effects of CRV431 on 28,278 genes, gene-variants, non-encoding microRNA and long RNA
- A study of genes and environmental interactions (epigenetics) may suggest specific genetic risk factors or specific genetic types of NASH.
- Decreased function of these genes is associated with NASH/NAFLD and fibrosis
- Bioinformatics will help guide clinical development of CRV431, and optimize for success

Gene	Implications for NASH (Down-regulation, loss-of-function, polymorphism)	Fold Change	p-value
TM6SF2	Linked to NASH and fibrosis	+4.2	0.0007
PNPLA3	Triacylglycerol hydrolysis: linked to NASH and fibrosis	+1.6	0.046
ApoB	Apolipoprotein of chylomicrons and LDL, ligand for LDL, linked to dyslipidemia, NASH and fibrosis	+10.9	0.0001
MTTP	Lipoprotein assembly: linked to NASH and fibrosis	+5.5	0.0003
GCKR	Linked to maturity-onset type 2 diabetes and NASH	+2.7	0.0036
LPIN1	Mutations associated with metabolic syndrome: linked to NASH and fibrosis	+1.9	0.01

ONGOING PHASE 2a AI-POWERED PILOT STUDY

OBJECTIVES

- Evaluate the safety and tolerability of once daily (qd) 75 mg and 225 mg dose of CRV431 in presumed nonalcoholic steatohepatitis (NASH) fibrosis stage 2 (F2)/fibrosis stage 3 (F3) patients compared to placebo control over 28 days of dosing
- Measure antifibrotic activity of CRV431
- Produce exploratory antifibrotic biomarker data: collagen biomarkers, matrix metalloproteinases, lipidomics, and genomics: Multi-Omic/Trait Data for use in AI-POWR™ Algorithm

STUDY DESIGN

- Multi-center (10 Sites), single-blind, placebo-controlled study
- Univariate Endpoints: AST, Pro-C3, ELF Score, Fibroscan

F2/F3 NASH Patients (n=36)

Cohort*	Fibrosis Stage	N	Day 1 – 28, fasted oral dosing	Day 29 - 42
A	F2/F3	12	CRV431 75 mg	Observation/Follow-up
B		6	Placebo	
C	F2/F3	12	CRV431 225 mg	
D		6	Placebo	

*randomized assignment; 2:1 – CRV431:placebo

Multivariate multi-omics-trait AI-POWR™ analysis to elucidate CRV431 activity biomarkers in F2/F3 NASH for Phase 2b Patient/Biomarker Selection

PHASE 2b AI-POWR NASH REGISTRATION TRIAL

OBJECTIVES:

- Evaluate the efficacy of once daily (qd) 75 mg and 225 mg dose of CRV431 in biopsy proven NASH fibrosis stages F2 and F3 patients compared to placebo over 6 months of dosing.
- Measure antifibrotic activity of CRV431
- Validate antifibrotic biomarker data: collagen biomarkers, matrix metalloproteinases, lipidomics, proteomics and genomics derived via AI-POWR Algorithm with clinical outcomes including a 1-point reduction in biopsy F score.

STUDY DESIGN:

- Multi-Center (28 US Sites), triple-blind, placebo-controlled (2:1), study
- Univariate Endpoints: AST, Pro-C3, ELF-Score, Fibroscan, biopsy histopathology
- Multivariate Endpoints: AI-POWR Multi-Omics Biomarker Panel confirmation and validation
- Enriched Design: Inclusion criteria includes AI-POWR Panel

F2/F3 NASH Patients (n=300)

Cohort*	Fibrosis Stage	N	6 Months	3 Month
A	F2/F3	100	CRV431 75 mg	Observation/Follow-up
B		50	Placebo	
C	F2/F3	100	CRV431 225 mg	
D		50	Placebo	

*randomized assignment; 2:1 – CRV431:placebo

Multivariate multi-omics-trait AI-POWR™ analysis to update CRV431 activity biomarkers in F2/F3 NASH for Phase 3 Patient/Biomarker Selection

ANTICIPATED EVENTS

CRV431

- Complete Ongoing Phase 2A NASH program (first dosing (75 mg) cohort completed November 2020)
  - ✓ Enrolled the last patient in the 75 mg cohort
  - ✓ DSMB recommended the study continue with 225 mg dose cohort
  - ✓ Clinically significant reductions observed in the liver safety parameters ALT and AST
  - Top line data for 75 mg cohort expected by end of Q4, 2020
- Complete long-term animal toxicology (Q2, 2021)
- Continue to optimize and scale-up chemistry and manufacturing (ongoing)
- Complete Additional Clinical Drug-Drug Interaction Studies (Q2, 2021)
- Prepare for NASH Phase 2B (to start mid-2021) using AI-POWR™ (ongoing)

AI-POWR™

- Continue to refine and extend AI-POWR™ for NASH and possible other indications (e.g., COVID-19)
- Continue to develop intellectual property (IP) for future CRV431 indications (e.g., additional fibrosis, viral disease) and business development strategies

CAPITALIZATION TABLE PRE-OFFERING

	As of September 30, 2020
Shares of Common Stock Outstanding	9,025,153
Series A Convertible Preferred Stock[1]	$855,810
Series C Convertible Preferred Stock[2]	$1,817,000
Warrants (WAEP $19.35)	2,536,566
Options (WAEP $5.96)	2,464,771

[1] Aggregate liquidation value. The Series A Convertible Preferred is convertible into 3,184 shares of common stock. Each share of Series A Convertible Preferred is convertible into that number of shares of common stock determined by dividing $10 (the stated value of such share) by $268.80. The Series A Convertible Preferred has no dividend rate.

[2]Aggregate liquidation value. The Series C Convertible Preferred is convertible into 16,747 shares of common stock. Each share of Series C Convertible Preferred is convertible into that number of shares of common stock outstanding by dividing $1,000 (the stated value of such share) by $108.50. The Series C Convertible Preferred has no dividend rate.

SUMMARY HIGHLIGHTS

- CRV431:
  - Safe and well-tolerated
  - Is currently in Phase 2a (Pilot) NASH patient study, 75 mg dosing cohort with first read-out expected Q4, 2020
  - Expected to initiate Phase 2b in NASH patients, mid-year 2021
- AI-POWR:
  - Expected to continue to drive CRV431 progress in NASH and potentially in additional indications
  - May be applied to identify novel/complementary collaborations/expansions
- Intellectual Property:
  - Continue to pursue and expand as warranted
- Use of Proceeds:
  - Fund our Research & Development activities and general corporate purposes

Nasdaq LISTED HEPA

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