# New Hope for Serious Infections

Maxim Group - Infectious Disease Virtual Conference Corporate Presentation May 2020



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or whether it will transform the care of BMT patients; whether the top line results of the STRIVE Part B clinical trial will be supported in the full analysis of the STRIVE Part B clinical data, and whether the success of the STRIVE Part B clinical trial or the post-hoc analysis of the STRIVE Part A and Part B data indicates a successful outcome in the Phase 3 ReSTORE clinical trial; and whether rezafungin could be effective for prophylaxis in COVID-19 patients. Certain statements regarding our Cloudbreak platform are also forward-looking including statements regarding whether our Cloudbreak platform can identify product candidates with intrinsic antimicrobial activity and immune engagement that will increase efficacy or represent an improvement over existing anti-viral agents; whether our AVCs for coronavirus will successfully inhibit viral fusion, identify therapies that are fast acting or provide long-acting prevention; whether Cidara's in-vitro data and/or clinical observations of other peptide inhibitors with a similar mechanism of action in HIV will be observed in any AVCs Cidara may advance to clinical development for coronavirus, whether the potential advantages of Cloudbreak AVCs observed in non-clinical studies for influenza will be observed in AVCs for coronavirus, whether AVC influenza candidates, including CD377, will achieve the major attributes believed to be needed in flu such as broad spectrum, superior resistance profile, protection for high-risk populations, expanded efficacy window, long duration of action and rapid onset of activity, or flexible administration; whether results observed in in-vitro and/or in-vivo animal studies with AVC influenza candidates, including CD377, will be observed in human use or represent an improvement over existing therapies; whether we will be able to advance CD377, or other influenza AVCs to clinical development or whether we will be able to

access BARDA funding; and whether our Cloudbreak platform can be expanded to identify product candidates to treat or prevent RSV, HIV, coronavirus or other viruses. This presentation also contains estimates and other statistical data made by independent parties and by Cidara relating to market size and growth and other data about Cidara's industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Projections, assumptions and estimates of the future performance of the markets in which Cidara operates are necessarily subject to a high degree of uncertainty and risk, including, Cidara's estimated use of proceeds from the Rights Offering; Cidara's ability to obtain additional financing; the success and timing of Cidara's preclinical studies, clinical trials and other research and development activities; receipt of necessary regulatory approvals for development and commercialization, as well as changes to applicable regulatory laws in the United States and foreign countries; changes in Cidara's plans to develop and commercialize its product candidates; Cidara's ability to obtain and maintain intellectual property protection for its product candidates; and the loss of key scientific or management personnel. These and other risks and uncertainties are described more fully in Cidara's Form 10-K as most recently filed with the United States Securities and Exchange Commission (SEC), under the heading "Risk Factors." All forwardlooking statements contained in this presentation speak only as of the date on which they were made. Cidara undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

# Cidara investment thesis

Leading science on long-acting antifungal and antiviral prevention and treatment

Rezafungin		1 <sup>st</sup> antifungal in 13 years for 1 <sup>st</sup> line treatment and prophylaxis
	Treatment – Phase 3	Transform treatment of candidemia and invasive candidiasis
	Prophylaxis – Phase 3	Transform prevention in high risk hematology (BMT) setting
	Validation	Significant ex-US/ex-Japan partnership with Mundipharma
Cloudbreak AVCs		Modular platform for viral protection & treatment
COVID-19 & Pan CoV		Rezafungin: Prophylaxis against invasive fungal infections Cloudbreak: Pre-clin testing new molecules against COVID-19

## Leading the science on antifungal & antiviral prevention & treatment

	1							
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Program	Proposed Indication	Discov.	in-vitro	in-vivo	enable	Ph 1	Ph 2	Ph 3

#### ANTIFUNGAL: Long acting treatment and prevention

Rezafungin	Treatment of Candidemia & Invasive Candidiasis			STRVE	
Rozarangin					
Rezafungin	Prophylaxis of IFD in Blood & Marrow				ReSPECT
Rozardingin	Transplant Patients				

#### ANTIVIRAL: Cloudbreak® Antiviral Conjugates (AVCs) for rapid treatment and long-term prevention

CD377	Influenza Single-dose/3months Prevention & Treatment				 
AVC108 Influenza Single-dose/6months Prevention & Treatment					 
RSV AVC	RSV Prevention & Treatment		<b></b>		 
HIV AVC	HIV PEP, PrEP, Maintenance			 	 
CoV AVC	COVID-19 & Pan CoV Prevention & Treatment			 	 

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# Cidara's pipeline targets multiple unmet medical needs

Rezafungin – Antifungal

Cloudbreak – Antiviral



# Rezafungin – Next generation antifungal in Phase 3

Possibly largest commercial opportunity in antifungal market

Unmet Need ICU, Chemotherapy and BMT, SOT patients at significant risk Mortality up to 60%<sup>1</sup> if infected *Candida:* no new treatment or prophylaxis for past 13 years

DifferentiationPhase 3 trials in largest first line segments of \$4.2B global market2ReSTORE: Transform treatment of *candidemia* and *invasive candidiasis*ReSPECT: Transform prevention in high risk hematology (BMT) settingSuperior time to fungal clearance3 and tissue penetration4, Once-weeklyNo observations of DDIs, QTc signal, myelosuppression or hepatotoxicity

Validation \$568M partnership with Mundipharma for ex-US/ex-Japan

\*ICU: intensive care unit; BMT: blood and marrow transplant, SOT: solid organ transplant, DDI: Drug-Drug Interactions, QTc: corrected QT interval on an electrocardiogram

<sup>1.</sup> The PATH (Prospective Antifungal Therapy) Alliance registry and invasive fungal infections: update 2012 (2012).

<sup>2.</sup> IQVIA, as of December 31, 2017

<sup>3.</sup> Data on file re superior time to negative blood culture vs caspofungin demonstrated in Phase 2 STRIVE trial

<sup>4.</sup> Unraveling Drug Penetration of Echinocandin Antifungals at the Site of Infection in an Intra-abdominal Abscess Model, Zhao et al, AAC July 2017

# Rezafungin in COVID-19 Patients

Aspergillosis may play a role in hyperimmune response and ARDS

#### Aspergillosis has been observed in up to 30% of severe COVID-19 patients<sup>1</sup>

- Pulmonary aspergillosis also occurs in 20% of severe influenza patients with 40-60% mortality<sup>2</sup>
- Similar pathogenesis in severe COVID-19 patients where use of immunosuppressants may increase the risk of aspergillosis

#### Does Aspergillus exacerbate the hyperimmune response and ARDS in COVID-19 patients?

- Increased IL-6 levels are correlated with increased rates of aspergillosis in COVID-19 patients
- Inflammation due to aspergillosis is also driven by IL-6, so the presence of *Aspergillus* in the respiratory tract may help drive the hyperimmune response and ARDS in COVID-19 patients

#### Rezafungin proposed as prophylaxis in a study in hospitalized COVID-19 patients

- Superior distribution to respiratory tract<sup>3</sup> and once-weekly dosing to limit healthcare interactions and enable earlier discharge vs daily echinocandins
- Lack of DDIs or QTc prolongation and favorable hepatic & renal safety profile vs SOC<sup>4</sup>

<sup>1. &</sup>quot;High prevalence of putative invasive pulmonary aspergillosis in critically ill COVID-19 patients", Alanio, Alexandre, et al, April 15, 2020 (https://ssrn.com/abstract=3575581)

<sup>2.</sup> Schauwvlieghe, et al, Lancet ID, 2018. Vanderbeke, et al,, Current OpinionI D, 2018. Wauters J, et al. Intens Care Med, 2012.

<sup>3.</sup> Unraveling Drug Penetration of Echinocandin Antifungals at the Site of Infection in an Intra-abdominal Abscess Model, Zhao et al, AAC July 2017

<sup>4.</sup> As observed in clinical development to date, including STRIVE Phase 2 trial

## Aspergillus exacerbates SARS-CoV-2 inflammatory response

Synergistic impact leads to vicious cycle of pulmonary inflammation and increased risk of death



Tay, M.Z., Poh, C.M., Rénia, L. et al. *Nat Rev Immunol* (2020). https://doi.org/10.1038/s41577-020-0311-8. Dagenais, T.R., Kelle,r N.P. *Clin Microbiol Rev.* 2009 Jul;22(3):447-65.

# Rezafungin: A novel echinocandin in Phase 3



#### Structural modification is designed to yield improved chemical & biological properties

- Designed for prolonged PK ------ once weekly dosing limit HC interactions
- Designed for high exposures ------ potential for improved efficacy
- Observed absence of toxic degradation products --- potential for improved safety
- No DDIs and favorable hepatic & renal safety ------ compatible with other medications

# Rezafungin overall phase 3 development plan

	<b>ReSTORE</b>	ReSPECT
	Phase 3 Treatment Trial	Phase 3 Prophylaxis Trial
Indication	Treatment of candidemia & invasive candidiasis in patients with limited treatment options	Prophylaxis against Aspergillus, Candida & PCP in allogeneic blood and marrow transplant patients
Phase 3 Size	184 patients <sup>2</sup> (20% NI margin)	462 patients (12.5% NI margin)
Overall objective	Enable early discharge of patients on a weekly echinocandin and outpatient use	Transform post-blood & marrow transplant standard of care

1. We plan to commence the ReSPECT trial initially in Europe and Canada.

2. Phase 3 Primary Evaluable Population size.

## STRIVE B Phase 2 data in candidemia & invasive candidiasis Corroborates STRIVE A results and supports ReSTORE Phase 3



# Rezafungin: Superior on time to negative blood culture

Time to negative blood culture (mITT population)



Data on file from STRIVE A and B combined

# 30-Day All Cause Mortality – Post Hoc Analysis\*

STRIVE Program: Rezafungin vs. Caspofungin



\* Using the same analysis method as planned for the Phase 3 study, a two-sided 95% confidence interval (CI) for the observed difference in the ACM rate (relevant Rezafungin group minus caspofungin group) was calculated using the unadjusted method of Miettinen and Nurminen.

Post-hoc analyses do not establish effectiveness and should not be assumed to establish the same outcome in Phase 3.

# Day 14 Clinical Response – Post Hoc Analysis\*

STRIVE Program: Rezafungin vs. Caspofungin



\* Using the same analysis method as planned for the Phase 3 study, a two-sided 95% confidence interval (CI) for the observed difference in the ACM rate (relevant Rezafungin group minus caspofungin group) was calculated using the unadjusted method of Miettinen and Nurminen.

Post-hoc analyses do not establish effectiveness and should not be assumed to establish the same outcome in Phase 3.

# **ReSTORE trial design mirrors STRIVE**



# Our partner for Rezafungin ex-US/Japan





# Rezafungin collaboration recognizes commercial potential



Ex-US; ex-Japan

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Melinta / Menarini: Vabomere, Orbactiv & Minocin

# Rezafungin overall phase 3 development plan

	<b>ReSTORE</b>	ReSPECT
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- 1. We plan to commence the ReSPECT trial initially in Europe and Canada.
- 2. Phase 3 Primary Evaluable Population size.

# The current standard of care is inadequate



1 Ullmann AJ et al. Posaconazole or fluconazole for prophylaxis in severe graft-versus-host disease. N Engl J Med. 2007 Jan 25;356(4):335-47.

2 Vasconcelles MJ et al. Aerosolzed Pentamidine and Pneumocystis Prophylaxis after Bone Marrow Transplantation is Inferior to Other Regimens and is Associated with Decreased Survival and Increased Risk of Other Infections, A. Society for BMT, 2000.

3 The PATH (Prospective Antifungal Therapy) Alliance registry and invasive fungal infections: update 2012 (2012).

# Rezafungin: potential simplified single drug paradigm

Antifungal prophylaxis in allogeneic blood and marrow transplant setting



# **ReSPECT Phase 3 prophylaxis trial design**



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# Cidara's pipeline targets multiple unmet medical needs

Rezafungin – Antifungal

Cloudbreak – Antiviral



# Vision for Antiviral Conjugates for respiratory disease: Single-dose treatment and long-acting protection

#### Against all strains...



<image>

# Cloudbreak antiviral platform: dual mechanism of action

Intrinsic antiviral activity & immune engagement



# Influenza & CoV-2 AVC program goals

#### A new class of long-acting drugs

*Not* a vaccine, monoclonal antibody or traditional therapeutic

A stable conjugate of a potent antiviral with an Fc antibody fragment

Rapid onset, potent activity coupled with 3-6 months of protection

#### CD377, (Flu AVC)



Universal treatment and prevention

- All seasonal and pandemic strains (A & B)
- Single-dose seasonal prevention
- Active in immunocompromised
- No evidence of resistance
- 54-fold safety window

'18-'19 Fl	u Season
Age	Flu VE
18–49	25%
50–64	14%
≥65	12%

Pan-coronavirus including CoV-2



Validated by flu and other AVC programs

- Prevents viral fusion to host cells
- Preclinical screening underway
- Goal: Pan-Coronavirus prevention or treatment, up to 6 months with 1 dose

# Cidara's Cloudbreak AVC platform

Proprietary engineered Fc domains provide dose and immune response options





# Coronavirus - Novel Cloudbreak AVC approach to treat & prevent



#### Novel Fc - peptide fusion AVC inhibitors for SARS and COVID-19

- Goal: fast-acting treatment and long-acting prevention
- 16 variants have been generated for first round of testing
- Several designs under evaluation
  - Broad spectrum activity against SARS, MERS and a-coronaviruses
  - Specific for COVID-19
- Peptide inhibitors with a similar MOA in HIV is clinically validated<sup>1</sup>
- At Cidara, an analogous Fc peptide fusion approach with HIV yielded potent (nM) *in-vitro* inhibitors of viral fusion

# Coronavirus AVCs are being designed to target viral fusion



# Potential Advantages of AVCs<sup>1</sup> in COVID-19

Utility for rapid treatment and long-term prevention of respiratory diseases

- Rapid onset of action
- Superior distribution to lung
- Months of protection from single dose
- Activity in immune compromised hosts

<sup>1.</sup> The above have been observed in preclinical testing of Cidara's AVCs under development for other therapeutics uses. To date, Cidara has not conducted similar *in-vivo* testing for its AVCs for COVID-19.

# CD377 for influenza: Validation of the approach in respiratory viruses

Broad spectrum, universal coverage

Superior resistance profile

Protection for High-Risk Populations

Expanded efficacy window

Long duration of action

Rapid onset of activity

Flexible administration



# Two mechanisms of action against the flu

CD377: A conjugate of a neuraminidase inhibitor with human Fc domain

Potent antiviral



#### Fc immune engager

#### 1. Inhibit viral proliferation

NA inhibition: Direct inhibition of viral proliferation



2. Immune-mediated clearance

Targeted clearance of infected cells



# Flu vaccines have well known limitations...



Strain-specific, variable coverage

10%-60% effective (2004-2018)<sup>1</sup>



Less effective in elderly & immune compromised

~2-week lag time to achieve full protection<sup>2</sup>

#### Manufacturing



Challenging in a pandemic: long, complex production

Difficult to scale, low yields can limit production capacity<sup>3</sup>

2. https://www.cdc.gov/flu/protect/keyfacts.htm

3. https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

... which place a substantial burden on the US population



The top range of these burden estimates are from the 2017-2018 flu season

Sources: CDC; https://www.cdc.gov/flu/about/burden/index.html Challenger, Gray, & Christmas, Inc.; <u>https://www.healthline.com/health/influenza/facts-and-statistics#5</u>

# ~320M people should be vaccinated/year in US



1. CDC.gov. Census Bureau 2017. Harpaz, Open Forum Infectious Disease Vol 3 Fall 2016

- 2. Respiratory co-morbidities include asthma and COPD
- 3. Other co-morbidities, driving higher risk, include all chronic conditions, but the major ones are diabetes, CV disease, etc.
- 4. Based on a 2018 US national survey commissioned by Research!America and American Society for Microbiology (N=1004), 53% people didn't get flu vaccine in last year, and 48% chose "do not trust flu vaccine" as the reason for not getting flu vaccine

# CD377 development candidate profile

Now in IND enabling studies

	Target Attribute	CD377
Indication	Universal prevention and treatment	All data are supportive
Spectrum	A & B + drug resistant strains, low resistance potential	Potent <i>in-vivo</i> activity against all seasonal and pandemic strains
Safety/Tolerability	High safety margin for long term prevention	> 54x exposure margin in 14-day primate toxicity studies
Dosing Frequency	1 to 2x per flu season	Estimated 3 to 6-month coverage with single SC or IM dose
Route of Administration	SubQ, IM and IV dosing	Equivalent exposures and efficacy
Target Populations	High risk populations where vaccines are not effective	Equally effective in immune compromised & immune competent models at similar doses

Data available at: https://www.cidara.com/wp-content/uploads/2020/03/Cidara-Cloudbreak-Deck-March-2020.pdf

# AVC Clinical Development Plan (Phase 1a)

Phase 1 Safety data to enable BARDA consideration

- Phase 1a- SAD/MAD (~1-year duration)
  - 3 dose groups (10:3 ratio of CD377 : Placebo) low, medium & high dose
  - Total follow-up of ~4 months following last dose



# Influenza Development Program

Two Indications- Treatment and Prevention

#### Treatment

- Potential advantages based on nonclinical data over current standard of care
  - Efficacy against all tested strains of Influenza A and B (including H1N1, H3N1, H5N1, H7N9, etc)
  - Efficacy against oseltamivir- and baloxavir-resistant strains
  - Improved efficacy with delayed dosing beyond 24 hours
- Proposed Trials
  - Phase 1b: Healthy volunteer challenge study (early POC)
  - Phase 2: dose-ranging in uncomplicated influenza
  - Phase 3: CD377 vs placebo, stratified for vaccine status
    - Focus will be on high risk outpatient or hospitalized, but could cover other influenza populations depending on regulatory interactions

# Influenza Development Program

Two Indications- Treatment and Prevention

### Prevention

- Potential advantages based on nonclinical data over vaccines
  - Superiority in high-risk patients with low vaccine efficacy: elderly, cardiac/pulmonary patients, and diabetics, transplant, and other immunosuppressed patients
  - Efficacy against all tested strains of Influenza A and B (including H1N1, H3N1, H5N1, H7N9, etc)
  - Efficacy against oseltamivir- and baloxavir-resistant strains
- Proposed Trials
  - Phase 1b: Healthy volunteer challenge study (early POC)
  - Phase 2: Dose-ranging in non-vulnerable population
    - Consideration for post-exposure prophylaxis study
  - Phase 3 (similar to vaccine studies in seasonal influenza): AVC vs Placebo in high-risk populations as defined in Table 4 of IDSA Guidelines

## **Financial overview**

Summary Consolidated	As of December 31, 2019					
Balance Sheet Information	As Reported	Pro Forma	Comment			
Cash and restricted cash <sup>1</sup>	\$60.3M	\$89.4M	PF includes rights offering proceeds of \$29.1M			
Common stock issued <sup>2</sup>	40.5M	51.5M	PF includes Series X pref. shares 'as converted'			
Pacific Western Term Loan	\$10.0M					

<sup>1.</sup> Includes \$60.3M of cash and restricted cash at December 31, 2019, and \$29.1M of net proceeds from the February 13, 2020 rights offering.

As Reported common stock as of February 25, 2020 (includes 6.6M shares of common stock issued in the \$30M rights offering on February 13, 2020). Pro forma includes

 (i) 40.5M shares of common stock and (ii) 11.0M shares of common stock issuable upon the conversion of Series X Convertible Preferred stock. Each share of Series X
 Convertible Preferred is convertible into 10 shares of common stock.

# Cidara is much more than a typical ID company

Strategic Focus	Transformative approaches to infectious disease
Rezafungin Treatment	Enable fast clearance of infection and early discharge vs SOC
Rezafungin Prophylaxis	Transform the care of BMT patients
Cloudbreak AVC	Radically different approach to viral treatment & prevention
Our Team	Experienced creators of shareholder value

# New Hope for Serious Infections

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