

# Bio-Path Holdings

An Oncology-Focused  
Biotechnology Company

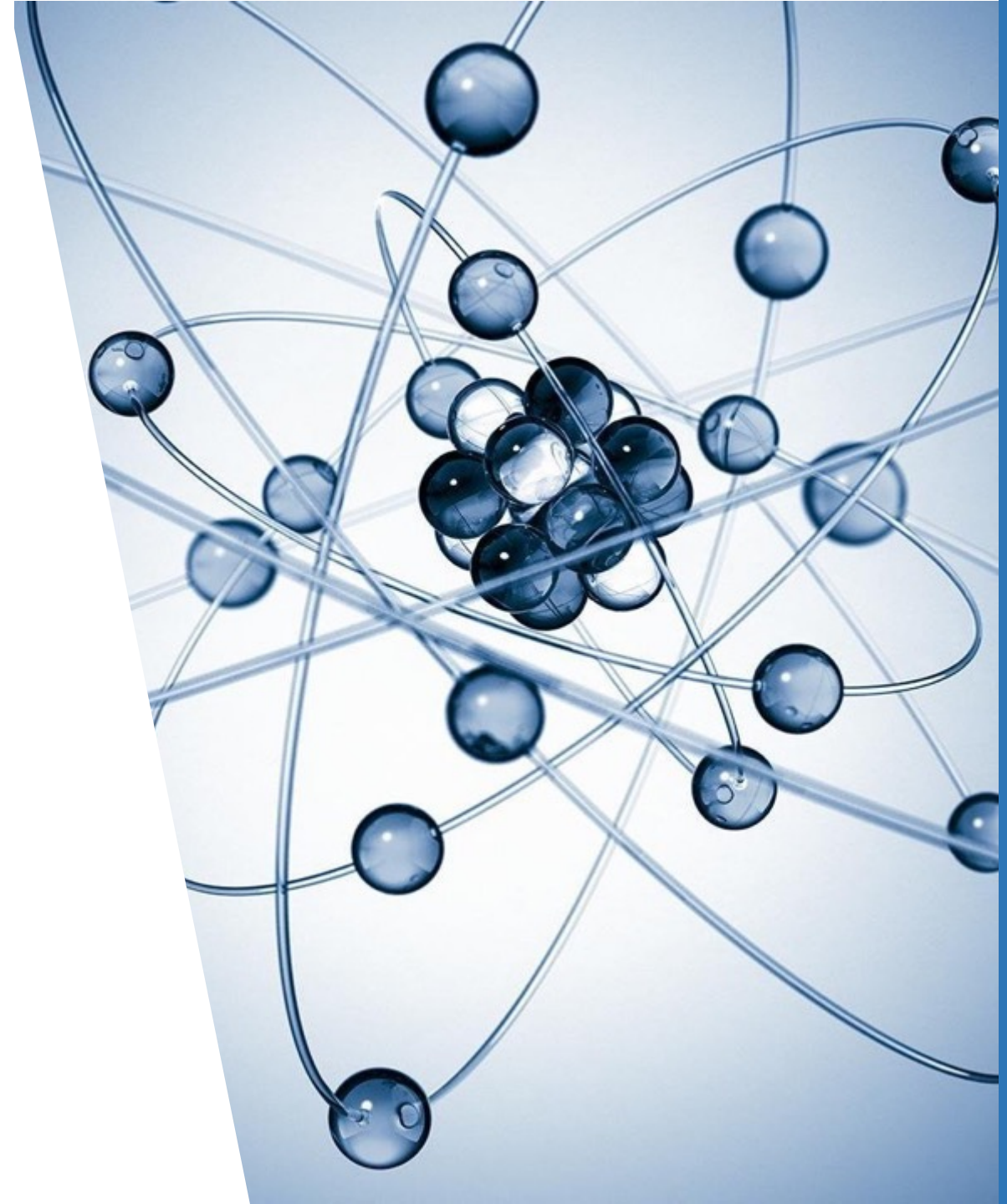
December 2018



# Forward looking statements

This Presentation contains forward-looking statements with respect to business conducted by Bio-Path Holdings, Inc. By their nature, forward-looking statements and forecasts involve risks and uncertainties because they relate to events and depend on circumstances that will occur in the future.

The Company does not undertake to update any forward-looking statements. There are a number of factors that could cause actual results and developments to differ materially and investors should use their own judgment to evaluate risks.



# Introducing Bio-Path Holdings

Advanced Oligonucleotide Therapeutics with  
High Efficiency Systemic Delivery

Publicly traded  
NASDAQ  
BPTH

Employees  
13

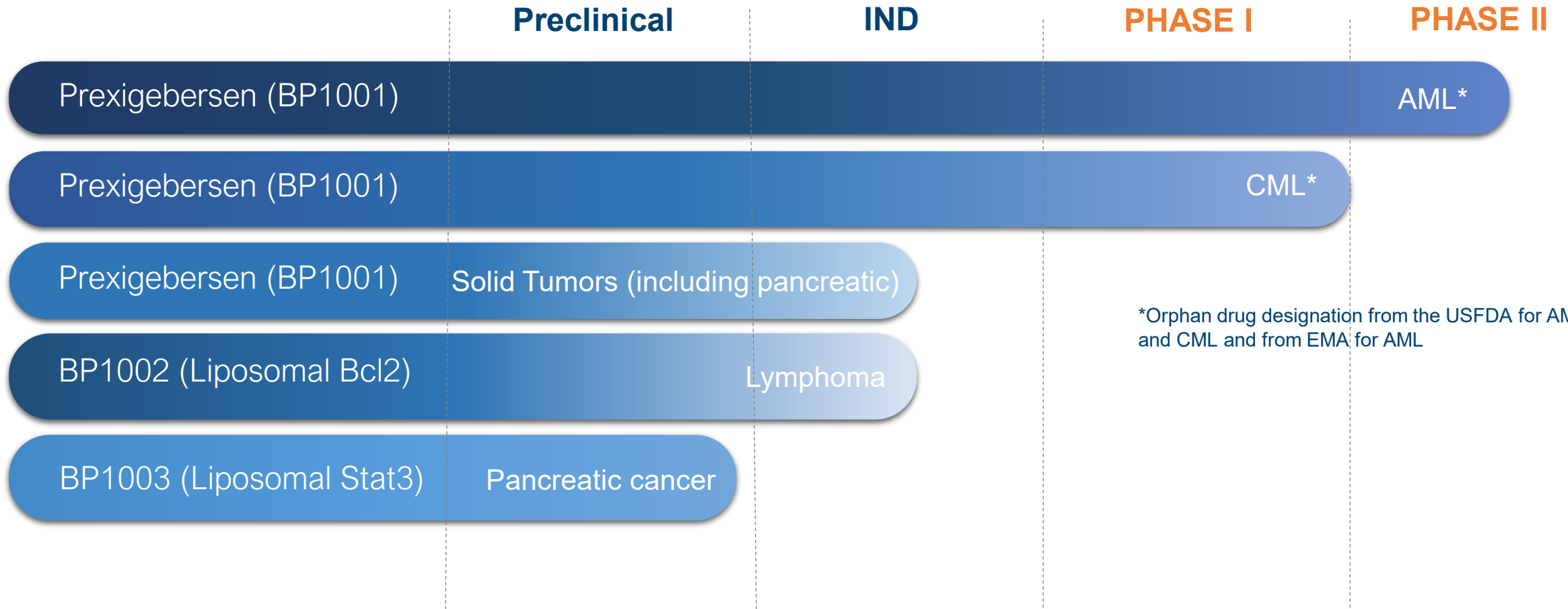
Established  
Houston, TX  
2007

**DNAbilize<sup>®</sup> Technology**, next generation single-stranded DNA antisense  
**Robust** clinical pipeline with novel oncology targets



## Technology Highlights

# Robust Oncology Pipeline



# DNAbilize<sup>®</sup> Technology

Proven As Safe, Robust and Targeted Method for Treating Disease

## No Toxicity

With human patients to date in Prexigebersen clinical trial.

- DNAbilize<sup>™</sup> liposome structure is similar to the cellular membrane
- P-ethoxy DNA does not induce hepatotoxicity or thrombocytopenia

## Systemic Treatment

I.V. delivery to the main organs via blood flow.

## High Cellular Uptake

Liposome structure is similar to the cellular membrane enhancing cellular uptake.

## Nanoparticle Liposomes

Enable penetration into tumors for delivery of drug.

## Proven Target Inhibition

Demonstrated that DNAbilize<sup>®</sup> method inhibits target protein, proving delivery technology works.



No Toxicity



Systemic Treatment



High Cellular uptake



Nanoparticle liposomes

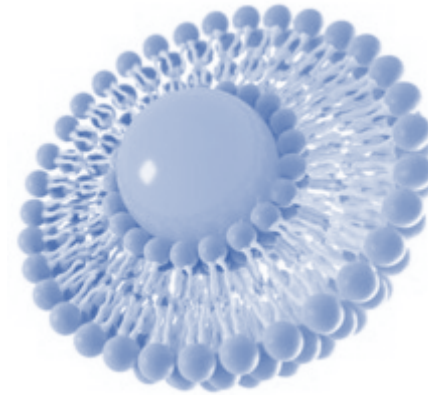


Proven target inhibition

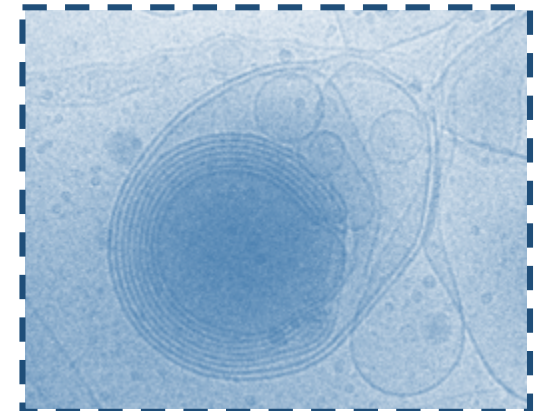
# DNAbilize<sup>®</sup> Technology

Nanoparticle Delivery Ensures Stabilization

- **Lack of surface charge** on lipid nanoparticle means avoidance of steric hindrance and **ensures cellular uptake**.
- **Slight hydrophobic nature** allows the oligonucleotide to incorporate readily into the lipid bilayers of a **neutral, uncharged lipid nanoparticle** forming **tight association and enabling safe delivery** throughout the body.
- **Nanoparticles are endocytosed** into the cells where the oligonucleotide is released.



Neutral liposome nanoparticle  
drive efficient cell delivery



# DNAbilize® Technology

Compared to other Antisense

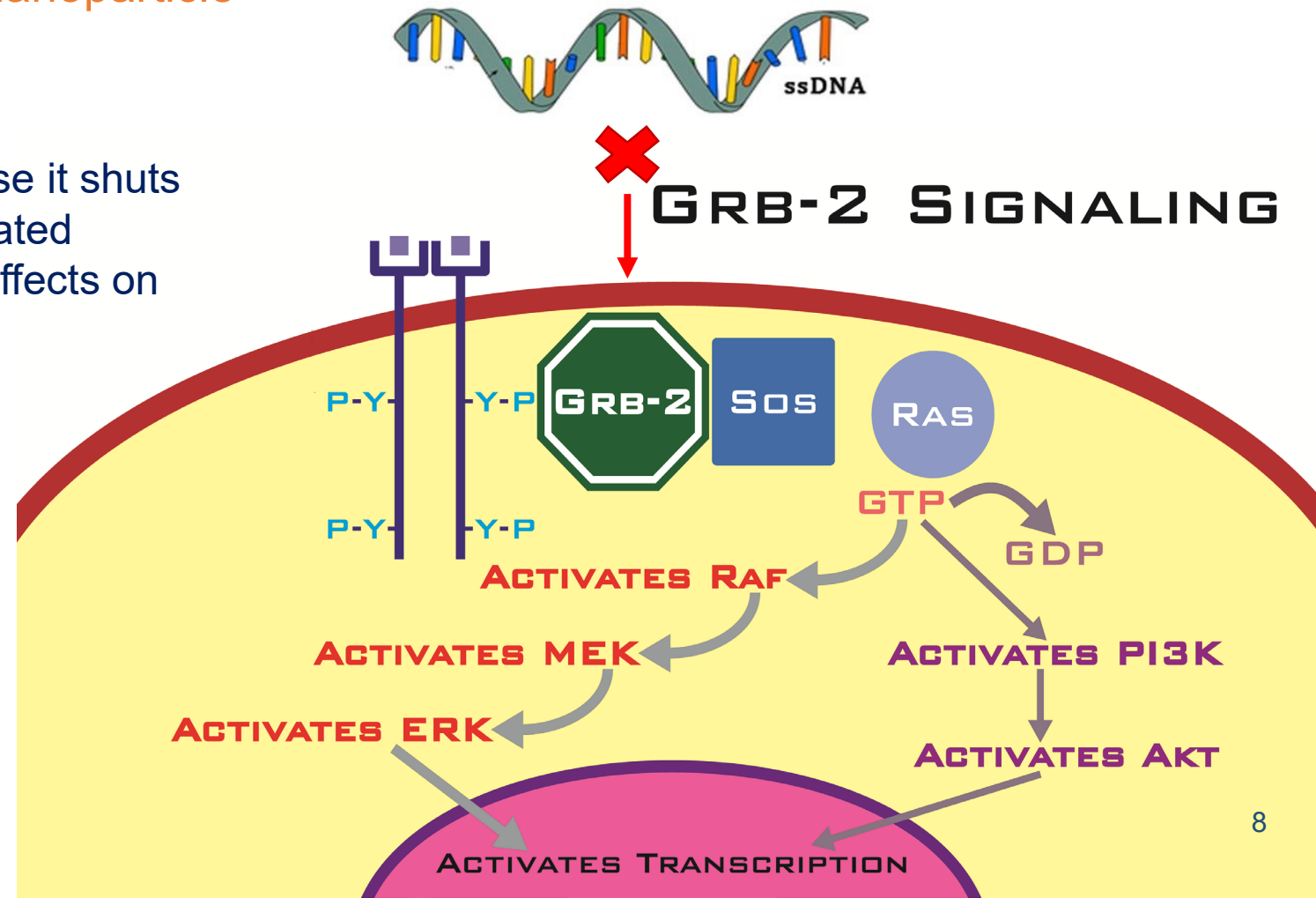
	1 <sup>st</sup> Generation	2 <sup>nd</sup> Generation	DNAbilize®	
No toxicity			✓	✓
Systemic Delivery			✓	✓
Target Specific	✓	✓	✓	✓
Effectiveness	✓	✓	✓	✓
High Cellular Uptake			✓	✓
Neutral charged stabilizing DNA backbone			✓	✓

Unlike other antisense technologies that demonstrate toxicities and poor cellular delivery, DNAbilize technology enables the development and delivery of **systemic** antisense RNAi nanoparticle treatments for a **broad spectrum** cancers and other diseases.

# DNAbilize® Lead Target and Indications: Grb2 and Myeloid Leukemia

Prexigebersen is an antisense RNAi nanoparticle targeting Grb2

- Ideal target for myeloid leukemia because it shuts down the Ras pathway in receptor activated myeloid cells without exerting adverse effects on Ras signaling through other channels





# Prexigebersen (BP1001): A Promising Treatment of Myeloid Leukemia

Prexigebersen in combination with LDAC is well-tolerated and shows early anti-leukemic activity in nearly 50% of evaluable AML patients in phase 2 studies

PK: 30 hour half life in plasma



No adverse effects attributed to Prexigebersen were observed



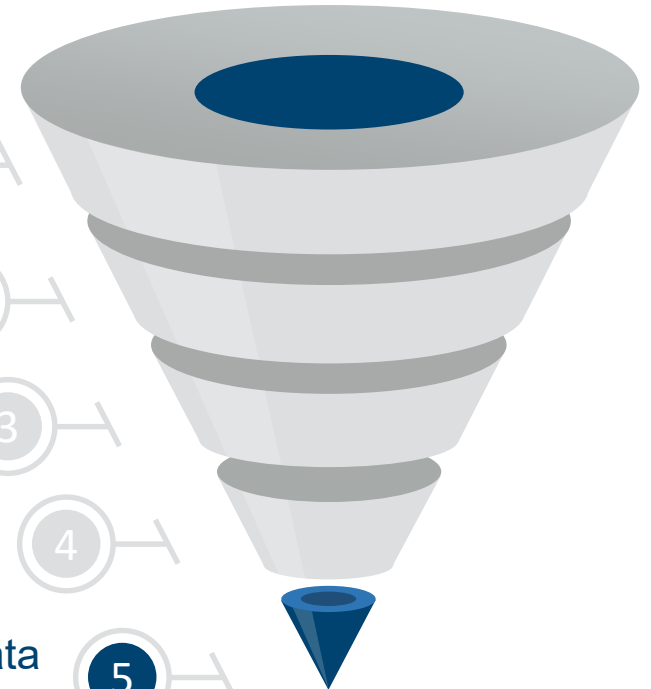
MTD was not reached as expected



71% average reduction of bone marrow blasts in responding patients



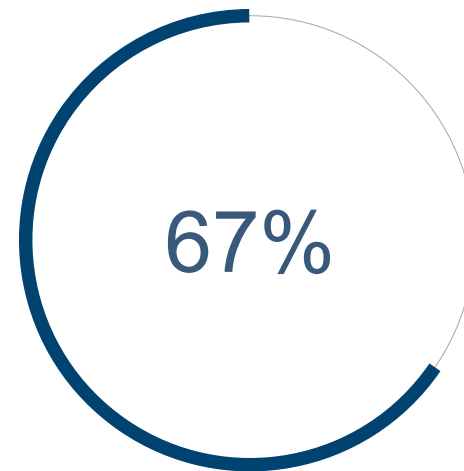
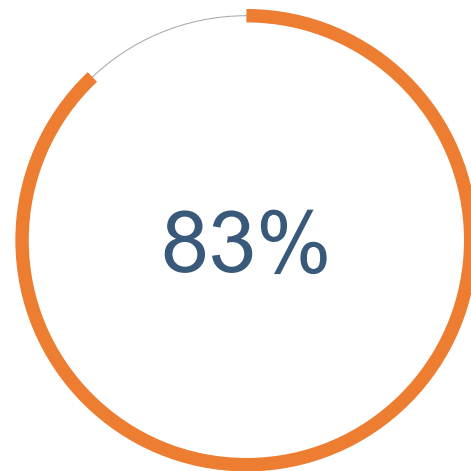
Newly planned protocol amendments may provide for pivotal study outcome data and hence, potential approvals in the US and Europe



# Summary of Phase I Monotherapy Clinical Trial Results for Prexigebersen

- N=39, AML, CML, & MDS Patients Refractory or Resistant to Current Therapies
  - Patients averaged 6 prior therapies
- Dose escalating treatment cycle, 8 doses over 4 weeks, up to 90 mg/m<sup>2</sup>
- **NO ADVERSE EVENTS/DRUG WAS WELL TOLERATED**  
One mucositis DLT occurred at the lowest dose (5 mg/m<sup>2</sup>) on the study in a patient with a history of prior exposure to hydroxyurea (hydroxyurea treatment continued during the study)

**Of the 18 evaluable patients with circulating blasts, 83% had a reduction in circulating blasts**



**Average reduction in circulating blasts was 67% in patients showing a decrease in bone marrow blasts**

# Prexigebersen Down-regulates Grb2 Protein in Target Cells

Grb2 levels decreased in 11 of 13 patient samples by end of treatment (EOT)  
 pErk levels decreased in 7 of 13 patient samples by EOT

Subject Number	Cohort	BP1001 Dose (mg/m <sup>2</sup> )	Grb-2 Decrease (Day 15)	pErk Decrease (Day 15)	Grb-2 Decrease (EOT)	pErk Decrease (EOT)
022	3	20	0%	0%	57%	0%
023	3	20	0%	3%	28%	45%
024	3	20	56%	28%	47%	35%
025	4	40	63%	82%	54%	91%
026	4	40	47%	0%	0%	0%
027	4	40	NS*	NS*	34%	27%
028	5	60	0%	0%	30%	54%
029	5	60	57%	51%	65%**	0%**
030	5	60	54%	55%	43%	47%
031	6	90	0%	0%	0%	0%
032	6	90	85%	54%	91%	63%
033	6	90	13%	13%	53%	2%
034	6	90	42%	42%	40%	0%

\*No sample collected

\*\*Fewer cells used in analysis because sample had less cells

# Phase I Conclusions

## Results support that Grb2 is a potential therapeutic target for haematological malignancies

- Favorable safety profile strongly suggests that BP1001 has a very different toxicity profile than other antisense oligonucleotide analogues, which have been associated with serum transaminase activation, thrombocytopenia, and activated partial thrombin time prolongation.
- The tolerability of BP1001 may prove useful in clinical combination settings
- Results published recently in *The Lancet Haematology* with Expert Commentary

### **The Lancet Haematology**

*“Liposomal Grb2 antisense oligodeoxynucleotide (BP1001) in patients with refractory or relapsed haematological malignancies: a single-centre, open-label, dose-escalation, phase 1/1b trial;”*

Volume 5, No. 4, e136–e146, April 2018

# Ongoing Phase II Efficacy Trial Design for AML Prexigebersen Combination Therapy

- Treatment of de novo AML patients who are induction therapy ineligible and unfit for stem cell transplant
- Efficacy trial will be conducted at up to 10 leading cancer centers in the U.S., including the MD Anderson Cancer Center; 6 sites have enrolled and treated patients
- Primary Endpoint: # patients who achieve CR, (accepted surrogate endpoint)



If IA is successful, the trial will expand to 54 patients. Plans for a pivotal trial will be discussed with FDA if results significantly exceed current therapy

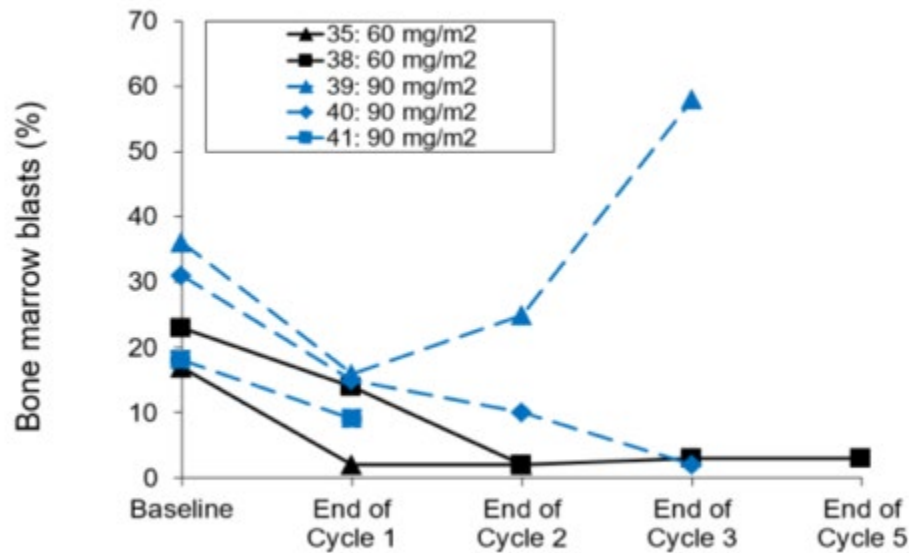
# Safety Segment Phase II Prexigebersen + LDAC Combination Therapy Show Encouraging Results

## Relapsed/refractory AML patients

- 3 evaluable patients per cohort, 2 cohorts, n=6
- Dose 60 mg/m<sup>2</sup> and 90 mg/m<sup>2</sup> respectively
- Received drug 2x week for 4 weeks per treatment cycle

## Encouraging Results

- 3 patients achieved **CR**
- 2 patients achieved **50% or greater bone marrow blast reduction with stable disease**
- Average age of Patients was 73.5 years old
- No Adverse Effects attributed to Prexigebersen
- No MTD reached

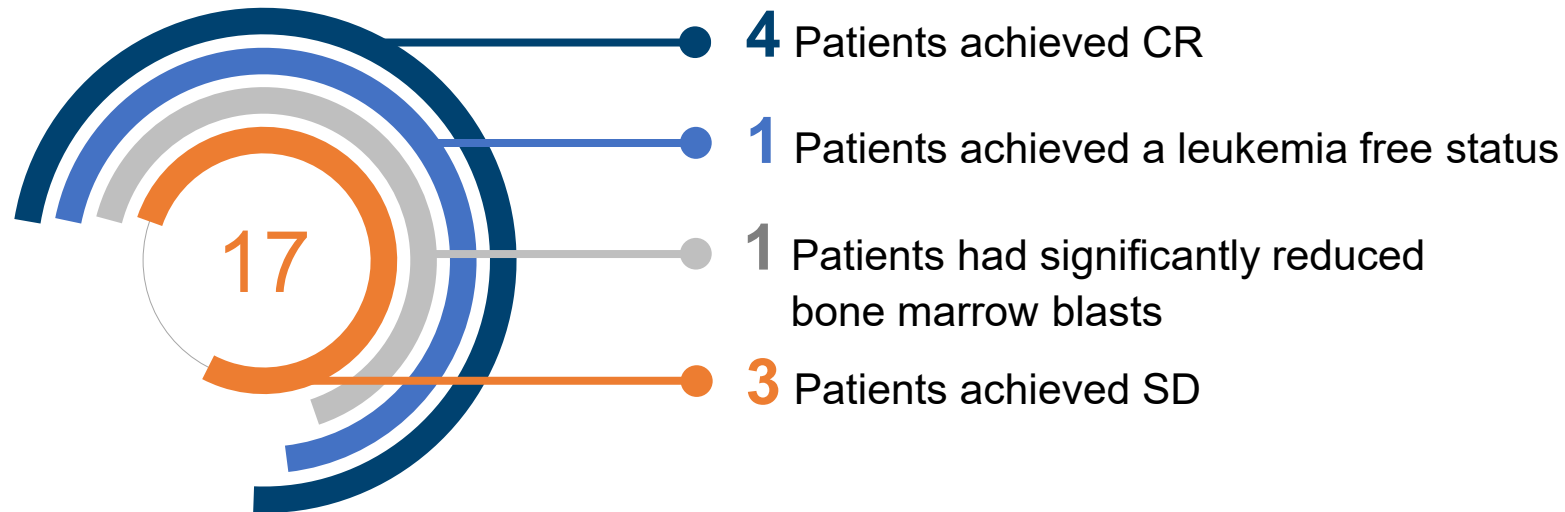


Patient	BP1001 (mg/m <sup>2</sup> )	BM Blasts % Reduction	Cycles completed	Response
35	60	88	1	CR
37	60	0	1	PD
38	60	91	5	CR
39	90	56	3	SD w/ ≥50% bmb reduction
40	90	68	3	CR
41	90	50	3	SD w/ ≥50% bmb reduction

**71% average Reduction of bone marrow blasts  
in responding patients**

# Results of Interim Analysis

## Patient evaluation summary



Of the evaluable patients showed some form of response, including CR and stable disease, to the combination treatment

Based on the recommendations of the study PIs, small protocol amendments will be made in the ongoing study

- Higher dose of Prexigebersen will be administered prior to LDAC treatment starting at day 10, instead of LDAC treatment starting at day 4
- The inclusion of decitabine cohort based on relatively new and positive data
- Study expanded to EU for both LDAC and Decitabine cohorts
- **Potential for 2 approvals!**

# Prexigebersen Advances To Phase II for CML Patients

Prexigebersen has the potential to treat the 33% of CML patients who are Gleevec resistant

- Prexigebersen (BP1001) decreased the proliferation of Gleevec resistant CML cells in a dose-dependent manner
- Prexigebersen pretreatment enhanced the inhibitory effects of Sprycel in CML cells, leading to cell death
- Two CML patients in Phase I with drug-resistant mutations showed significant reductions in circulating blasts

*American Society of Hematology Annual Meeting, "BP1001, a Novel Therapeutic for Chronic Myelogenous Leukemia," Dec 2016*





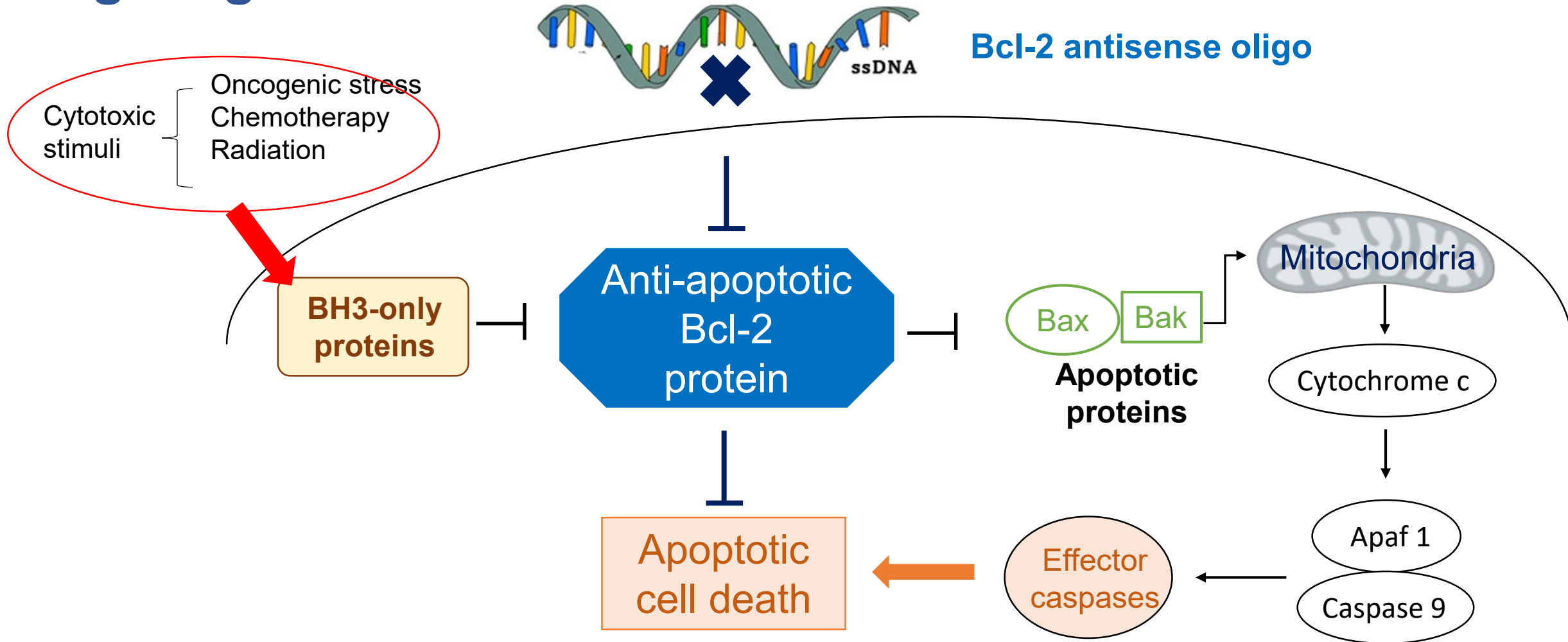
## Phase II CML Clinical Program: Open For Enrollment

- Determine if there is a DLT of Prexigebersen in combination with Sprycel
- 2 cohorts of 3 evaluable patients (n=6) at 60 mg/m<sup>2</sup> and 90 mg/m<sup>2</sup>
- Compare the efficacy of Prexigebersen in combination with Sprycel to historical response rates in blast phase and accelerated phase CML patients

## Prexigebersen Advances Towards Phase I Study For Solid Tumors

- Prexigebersen decreased ovarian tumor burden by 86% and multinodular burden in mice compared to control, with no apparent toxicity
- Prexigebersen enhanced paclitaxel efficacy against ovarian tumor progression
- Now preparing for a Phase I trial of Prexigebersen in several solid tumor types, including ovarian cancer and potentially pancreatic and triple negative breast cancers!!

# BP1002 is an antisense RNAi nanoparticle targeting Bcl-2



By blocking Bcl-2 protein expression, BP1002 allows cytotoxic stimuli, such as oncogenic stress, chemotherapy, and radiation, to activate the Bax/Bak-mediated apoptotic pathway.

# BP1002 Summary

- BP1002 decreased viability of lymphoma cells (11 of 15 lymphoma cell lines)
- BP1002 extended survival of mice bearing lymphoma xenografts
- Completed IND-enabling studies (pharmacokinetics, rodent toxicology rabbit toxicology, genotoxicity, BCL-2 flow cytometry)
- IND preparation underway



# Experienced Leadership Team



**Peter Nielsen**

**Co-Founder, President,  
Chief Executive Officer  
and Chief Financial  
Officer**

**Officer and Director  
since founding  
Company in 2007**

Manufacturing  
development and  
evolution of engineered  
product design



**William Hahne, M.D.**

**Vice President of  
Clinical Research**

**Medical consultant for Medimmune,  
Lion Biotechnologies, Seattle  
Genetics, Aminex Therapeutics,  
Therakos, and Celgene Cellular  
Therapeutics**

Held executive positions in clinical research  
and medical affairs at Celator  
Pharmaceuticals, Celsion Corp, and CurGen



**Ana Tari Ashizawa,  
PhD, MBA**

**Vice President, Research  
& Development**

**Key member of the  
research team that  
developed our  
liposomal delivery  
technology**



**Anthony Price,  
MBA**

**Vice President, Finance  
& Accounting**

**Former Associate Director of  
Accounting and Finance at  
Lexicon Pharmaceuticals**

# Scientific Advisory Board



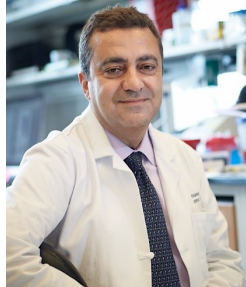
**Jorge Cortes, M.D.**  
Chairman

- M.D. from la Facultad de Medicina, Universidad Nacional Autónoma de México
- Jane and John Justin Distinguished Chair in Leukemia Research, Chief of the AML and CML sections, and Deputy Chair of the Department of Leukemia at The University of Texas MDACC
- Has consulted leading pharmaceutical companies such as AstraZeneca on development of prenyltransferase inhibitors, GlaxoSmithKline on the use of topotecan in MDS and CMML, and Rhône-Poulenc Rorer on the use of PEG-Asparaginase in adult ALL



**D. Craig Hooper,**  
Ph.D.

- Professor of Cancer Biology and Neurological Surgery and the Section Chief for Translational Research, Tumor Division, in the Department of Neurological Surgery at Thomas Jefferson University
- His work has led to novel immune therapies for rabies infection, neuro-inflammation, and cancer with 10 issued U.S. patents and 19 international patents that have been licensed to five companies in the U.S. and abroad
- He is the founding president of the Jefferson Chapter of the National Academy of Inventors and a fellow of the National Academy of Inventors.



**Anas Younes, M.D.**

- Professor and chief of the Memorial Sloan Kettering's Lymphoma Service. He has an extensive background in translational scientific research with a particular interest in targeted therapies.
- More than 20 years career at M.D. Anderson Cancer Center, most recently as director of clinical and translational medicine in the department of lymphoma and myeloma.
- Medical degree from the University of Damascus School of Medicine. He completed his internal medicine residency training at SUNY Downstate Medical Center and his pathology residency at the Medical College of Ohio. He completed his hematology fellowship training at Memorial Sloan Kettering.



**Jason B. Fleming,**  
M.D., F.A.C.S.

- Newly appointed Chair of the Department of Gastroenterology at H. Lee Moffitt Cancer Center and Research Institute.
- Professor with tenure in the Department of Surgical Oncology at the University of Texas MD Anderson Cancer Center in Houston.
- Served as as chief of Pancreas Surgery and executive director of Perioperative Services and created the first xenograft program in gastrointestinal cancer.
- Received the Castle Connolly Top Doctor award every year since 2013
- President's Faculty Recognition Award for Outstanding Contribution to the University of Texas MD Anderson Cancer Center in 2016.

# IP, Financial Snapshot and Upcoming Milestones

## Intellectual Property

- Original patents licensed from MD Anderson
- New composition and methods of use patent issued covers DNAbilize<sup>®</sup> technology, solely owned by Bio-Path: Five additional patents pending

## Financial Snapshot

- **Ticker:** NASDAQ: BPTH
- **Cash:** \$2.3 million as of September 30, 2018
- **Market Cap:** Approximately \$3-5 million
- **Burn rate:** Approximately \$1.5 million per quarter

## Upcoming Milestones

- Interim assessment AML Phase 2
- Phase 2 CML safety segment readout
- IND BP1002
- IND solid tumors

# Bio-Path Holdings

Thank you for your attention

Bio-Path Holdings, Inc.  
4710 Bellaire Blvd Suite 210 Bellaire, TX 77401  
Web: [www.biopathholdings.com](http://www.biopathholdings.com)  
Mail: [partnering@biopathholdings.com](mailto:partnering@biopathholdings.com)  
Tel: (832) 742-1369