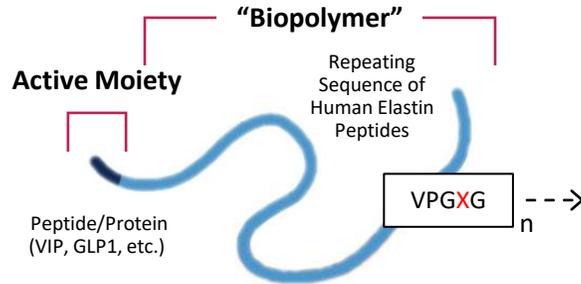


Safety, Tolerability, and Changes in Six-Minute Walk Test After Open-Label Subcutaneous PB1046, A Sustained-Release Analogue for Vasoactive Intestinal Peptide (VIP), in Pulmonary Arterial Hypertension (PAH)

 Sumita Paul, MD, MPH, FACC¹, Raymond L. Benza, MD, FACC², Murali Chakinala, MD³, Priscilla Correa⁴, MD, Kalyan Ghosh¹, PhD, John Lee¹, MD, PhD, and James White⁵, MD
¹ PhaseBio Pharmaceuticals, ² The Ohio State University Wexner Medical Center, ³ Washington University School of Medicine, ⁴ Allegheny Health Network, ⁵ University of Rochester Medical Center

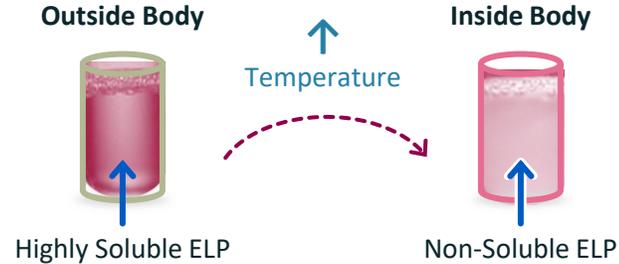
PB1046 (Pemziviptadil) – VIP Analogue

PROLONGED CIRCULATING HALF-LIFE



UP TO 200x INCREASE IN ½ LIFE

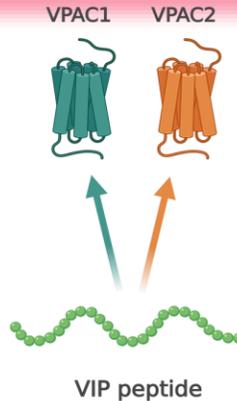
COACERVATION DELIVERS SLOW RELEASE



WEEKLY OR MONTHLY DOSING

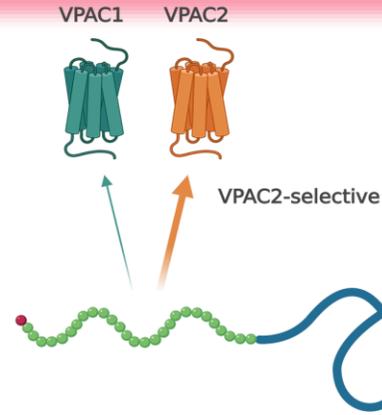
Pemziviptadil is an investigational neuropeptide, VIP, genetically fused to an elastin-like biopolymer for treatment of PAH:

- Confers a prolonged circulating half-life with coacervation delivering slow release of VIP.
- The biologic effects are mediated by two receptors, VPAC1 and VPAC2, belonging to the family B of G protein-coupled receptors in the pulmonary and systemic circulation.
- Functional deficiency of VIP has been described in humans with PAH.



Half-life ~1 Minute in Humans

Endogenous VIP



Half-life ~60 Hours in Humans

Pemziviptadil

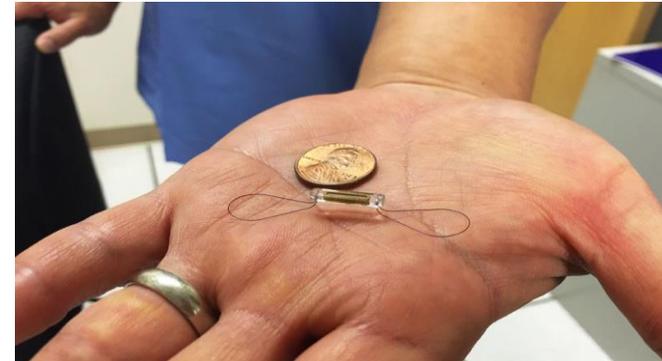
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Methods:

- The multi-dose safety, PK, and VIP-based functional and pharmacodynamic effects of Pemziviaptadil were evaluated in an open-label, multi-dose study in three female PAH subjects with an implanted CardioMEMS™ device.
- The safety and accuracy of the CardioMEMS™ HF System, which continuously monitors pulmonary artery pressure from a sensor implanted into the pulmonary artery, have been previously documented, along with correlations with Swan-Ganz measurements and echocardiography.
- Pemziviaptadil was administered weekly subcutaneously x 8 weeks (extended due to subjective improvements) at dose levels previously tested and shown to be safe.
- We have [previously reported](#) the hemodynamic changes. This report describes the changes in functional capacity based on the results of the six-minute walk test distance.

The CardioMEMS™ HF System



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Subject	Age (years)	6MWT at Baseline	6MWT at Follow up	Change from Baseline	Duration of Treatment
#1	74	220 meters	236 meters	+ 16 meters	6 months
#2	29	468 meters	546 meters	+ 78 meters	18 months
#3	61	411 meters	402 meters	- 9 meters	2 months

Results:

- Pemziviaptadil was well tolerated.
- PK profile data confirmed the dose-related but less than dose proportional increase in study drug exposure observed in humans with essential hypertension.
- The 6MWT distance improved after 18 months of treatment in a 29-year-old woman; it was approximately stable in the other two participants without any clinically meaningful deterioration.

Conclusions:

- The preliminary data for Pemziviaptadil support continued evaluation as a potential novel therapy for PAH patients.
- Pemziviaptadil appears to be safe and well tolerated.
- These hypotheses will be tested in the ongoing randomized, double-blind, parallel group Phase II PAH study assessing exercise capacity after 16 weeks of Pemziviaptadil.