



## TECHNOLOGY

# Targeting Protein Translation with Novel Small Molecules for Treating Pancreatic and Prostate Cancer

## OVERVIEW

Medicinal chemists at UMB designed a family of **novel small molecules** which block key drivers of the protein translational complex by **degrading MNK1/2** (i.e., mitogen-activated protein kinase (MAPK)-interacting kinase 1/2), thus inhibiting the activation of the eIF4E axis and inhibiting tumor growth. Lead compounds designated “**VNPP414**” and “**VNPP433-3?**” are promising candidates for the treatment of prostate (PC) and pancreatic cancer (PANC). Originating from Prof. Njar’s group at University of Maryland, Baltimore was an earlier drug candidate (“galeterone”), which was well tolerated in clinical studies and advanced to a Phase III trial for the treatment of patients with castration-resistant prostate cancer. The new leads VNPP414 and VNPP433 described here are chemically related to galeterone.

In a study with leads VNPP414 and VNPP433 (*Kwegyir-Afful et al., Oncotarget 2017*), both compounds inhibited cell viability of gemcitabine-naïve and gemcitabine-resistant PANC cells, and potentiated the effects of gemcitabine treatment in both cell types. *In vivo* treatment with each compound inhibited tumor growth in PANC tumor xenografted mice, with tumor growth inhibition ranging from 80% to 92%, compared to controls. When measuring the efficacy of the compounds as %T/C, the growth inhibition ranged from 8.1 to 19.4%T/C, classifying these agents as highly efficacious according to criteria set by the National Cancer Institute. In xenograft mouse models of castration-resistant prostate cancer, lead compounds VNPP414 and VNPP433 as well as VNPT55 suppressed tumor growth, including in treatment-resistant tumors expressing AR-V7 (*preliminary data*).

## CONTACT INFO

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## Additional Information

### INSTITUTION

University of Maryland, Baltimore

### PATENT STATUS

Issued Patents | U.S. Patent 9,694,005, JP Patent 6417392, AU Patent 2014247941, CA Patent 2,908,557, UK, FR, GR Patent 2991644

### LICENSE STATUS

Available

## CATEGORIES

- Therapeutics
- Small molecules

## INVESTIGATOR(S)

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Andrew Kwegyir-Afful  
Francis Murigi

## ATTACHMENTS

-  [Download Njar summary Gal analogs \(VN-2013-094; 6-2-19\).pdf](#)

## EXTERNAL RESOURCES

- [Ramamurthy \(2017\). Curr Opin Oncol. 29\(3\):210-220](#)
- [Kwegyir-Afful \(2016\) FEBS. 283\(21\):3898-3918](#)
- [Kwegyir-Afful \(2017\) Oncotarget](#)

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