



PURDUE  
INNOVATES

Office of Technology  
Commercialization

# Telescoped Continuous Flow Synthesis of an AlkynylNaphthyridine Anticancer Agent, HSN608

**New activity-based probes offer enhanced sensitivity and cell-based compatibility for high-throughput screening and identifying proteasome stimulators and inhibitors.**

Researchers at Purdue University have developed a new high-throughput method for continuous synthesis of an alkynylNaphthyridine anticancer agent, HSN608. HSN608 is a drug agent that shows promise as a treatment for Fms-like tyrosine kinase 3 (FLT3) driven cancers including acute myeloid leukemia (AML). There remains an unmet need to safely scale-up production of HSN608. Its synthesis requires complex amide and Sonogashira coupling reactions that are traditionally catalyzed by dangerous reagents such as palladium and copper, which can lead to creation of explosive byproducts. In addition, liquid chromatography-mass spectrometry (LC-MS) is currently used to validate the composition of HSN608 during its synthesis but is limited to analyzing 384 reactions in 33 hours. Purdue researchers implement desorption electrospray ionization-mass spectroscopy (DESI-MS), which can analyze up to 6,144 reactions in less than 2.5 hours, to optimize reaction conditions. The optimized reaction safely and rapidly induces amide and Sonogashira coupling through a two-step telescoping sequence to quickly synthesize HSN608. The new high-throughput microscale technique achieves 10-fold higher workload and 5-fold higher reduction in catalyst and co-catalyst loading steps, enabling approximately 8 mg of HSN608 to be produced per hour in up to 55 hours of continuous operation.

## Advantages:

- Safe
- Cost-Efficient
- Scalable
- Continuous Production

**Technology ID**  
2020-THOM-69095

**Category**  
Biotechnology & Life Sciences/Biomarker Discovery & Diagnostics  
Chemicals & Advanced Materials/Specialty & Performance Chemicals  
Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation  
Pharmaceuticals/Pharmaceutical Manufacturing & Methods  
Pharmaceuticals/Research Tools & Assays

**Authors**  
Shruti Biyani  
Qingqing Qi  
Herman O Sintim  
David Harley Thompson

**Further information**  
Joe Kasper  
[JRKasper@prf.org](mailto:JRKasper@prf.org)

Nathan Smith  
[nesmith@prf.org](mailto:nesmith@prf.org)

[View online](#)



Potential Applications:

- Drug Discovery
- Life Science Research
- Chemical Synthesis

**Technology Validation:**

The two-step telescoping sequence used to promote amide and Sonogashira coupling has been validated with DESI-MS as well as subsequent HSN608 product yield (8mg/hour). The system has also been tested in continuous operation for up to 55 consecutive hours.

Recent Publication:

"Use of High-Throughput Tools for Telescoped Continuous Flow Synthesis of Alkynylnaphthyridine Anticancer Agent, HSN608"

Journal of Organic Process Research & Development

American Chemical Society

DOI: 10.1021/acs.oprd.0c00289

**TRL:** 4

**Intellectual Property:**

Provisional-Gov. Funding, 2020-05-19, United States | PCT-Gov. Funding, 2021-05-13, WO | NATL-Patent, 2021-05-13, Europe | NATL-Patent, 2022-11-18, United States

**Keywords:** High-throughput synthesis, continuous flow synthesis, alkynylnaphthyridine, HSN608, anticancer agent, DESI-MS, Sonogashira coupling, amide coupling, chemical synthesis, continuous production