

Filed On Behalf Of:

C4 Therapeutics, Inc.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

C4 THERAPEUTICS, INC.
Petitioner

v.

FOGHORN THERAPEUTICS, INC.
Patent Owner

PGR No.: To Be Assigned
U.S. Patent No. 11,560,381

DECLARATION OF
KEVIN TYLER SPROTT, PH.D.,
UNDER 37 C.F.R. §1.68 AND §42.53(a)

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I. INTRODUCTION

I, Kevin Tyler Sprott, Ph.D., hereby declare as follows:

1. My name is Kevin Tyler Sprott, Ph.D. I am the Head of Tesova Drug Discovery Consulting LLC. My Curriculum Vitae is provided as Attachment 1 to my Declaration.

2. I have been retained by Knowles Intellectual Property Strategies, LLC on behalf of C4 Therapeutics, Inc. (“C4T” or “Petitioner”) as an independent expert to provide my opinions on the claimed subject matter in U.S. Patent No. 11,560,381 (the “’381 Patent”) (Ex.1001).

3. I am an expert in complex organic synthesis. My experience includes synthetic chemistry research with Nobel Laureate Elias J. Corey as a Post-Doctoral Fellow at Harvard University. Prior to my work with Professor Corey I received my Ph.D. from the University of Kansas under Professor Paul R. Hanson in 2001 and my B.Sc. in Biology as well as a B.A. in Chemistry from Wake Forest University in 1995.

4. I launched my industrial career as a research organic chemist at Millennium Pharmaceuticals (now Takeda Oncology Company) where I was involved in the synthesis, discovery and identification of three pharmaceutical products selected for clinical development (pevonedistat, MLN6095, and MLN0905). Pevonedistat has been the subject of over a dozen clinical trials.

5. I then joined Ironwood Pharmaceuticals (now Cycleron) in 2006 as a Principal Investigator. At Ironwood I was involved in the synthesis, discovery and development of several small molecule pharmaceutical development candidates including IW-6118, IW-7229, and IW-1221. I led project teams across various clinical indications including multiple sclerosis, asthma, pain, and inflammation. I also chaired the Small Molecule Program Advisory Committee.

6. In 2011 I left Ironwood Pharmaceuticals to co-found Verastem, Inc. as Senior Director of Chemistry. At Verastem I hired and managed teams of organic chemists in the United States, China, and Canada. I was involved in the synthesis, discovery, and selection of several lead compounds and in identifying which compounds were appropriate for in-licensing or acquisition. I also held the role of Head of Internal Intellectual Property and managed the procurement of IP over a portfolio of over 22 patent families. Verastem had a successful initial public offering in 2012.

7. In 2013 I joined Syros Pharmaceuticals as a Senior Director of Chemistry and an initial member of the management team. At Syros I led, hired, and managed multi-disciplinary teams of organic chemists and other scientists to synthesize and evaluate anti-cancer treatments. Syros Pharmaceuticals had a successful initial public offering in 2016. I also led the primary internal program, which was a CDK7 inhibitor, from conception through Phase 1 clinical study.

8. In 2018 I joined the SMOC Therapeutics Board of Directors and served as Senior Vice President. At SMOC I led scientific strategy and operations which resulted in the identification of organic chemical compounds in three early-stage drug discovery programs. I also recruited and hired medicinal chemists to aid in SMOC's drug discovery efforts. SMOC Therapeutics was acquired by Ventus Therapeutics which still employs the foundational science built at SMOC.

9. In 2021 I co-founded Stablix, Inc. I was the Chief Operating Officer of Stablix and had a primary role raising initial capital (\$78M series A) and building teams of organic chemists and other scientists to synthesize and evaluate heterobifunctional compounds to stabilize target proteins. Stablix is a leader in the field of heterobifunctional compounds for the stabilization of target proteins. These molecules are related to the heterobifunctional degraders but instead of degrading proteins they stabilize them by removing ubiquitin.

10. Throughout these experiences I have had a principal role in the scientific pursuit and capital raise in connection with new organic small molecule therapeutic agents. I have also managed and selected scientists for various roles and responsibilities, including synthesis and evaluation and am thus familiar with the level of skill possessed by a person of ordinary skill in pharmaceutical sciences.

11. A list of my publications, presentations, and patents is provided in Attachment 1.

12. I understand that C4 Therapeutics, Inc. is challenging the granted patent claims of the '381 Patent as Petitioner in a Post Grant Review proceeding at the Patent Trial and Appeal Board ("PTAB"), and that it is asking the PTAB to cancel all of claims 1-12 of the '381 Patent on the grounds of violation of 35 U.S.C. §112(a), 35 U.S.C. §112(b), and 35 U.S.C. §102. My Declaration focuses on whether a Person of Ordinary Skill in the Art ("POSA") would conclude the claims as issued are sufficiently enabled to practice the invention (35 U.S.C. §112(a)) and whether a POSA would consider the scope of the claims definite enough to determine whether a compound of interest infringes the claims (35 U.S.C. §112(b)). These laws have been explained to me, as discussed below.

13. I am being compensated for my time at a rate of \$650 per hour. My compensation does not depend on my opinions, conclusions, or the outcome of this proceeding. I am over 21 years old and competent to provide this Declaration.

II. SCOPE OF WORK AND SUMMARY OF OPINIONS

14. I have been asked by Petitioner to act as an independent expert to review the '381 Patent to (1) determine whether the claims of the '381 Patent are enabled across their scope; (2) draw representative compounds covered by the '381 Patent claims; and (3) consider whether a POSA would have difficulty determining whether a compound of interest falls within the scope of the issued claims.

15. Based on my review of the '381 Patent I determined that the claimed scope of compounds is not enabled as it covers far too many non-operative compounds and there is insufficient guidance in the application on how to make or use the vast chemical space covered by the claims. I also conclude that a POSA would not be able to determine whether certain compounds of interest infringe the claims.

III. PERSON OF ORDINARY SKILL IN THE ART

16. The legal standards used in this opinion have been explained to me by counsel. I understand that issues I address in this Declaration should be evaluated from the perspective of the person of ordinary skill in the art ("POSA"). I discuss the perspective of a POSA in the paragraph below and the remaining legal standards are provided in Section VI.

17. I have reviewed the definition of a POSA provided by Dr. Djuric and based on my experience in medicinal chemistry I agree with his definition of a POSA. Specifically, a POSA would have (a) a Ph.D. in chemistry, medicinal chemistry, biochemistry, or a closely related discipline in the pharmaceutical area or (b) an M.S. degree in chemistry, medicinal chemistry, biochemistry, or a closely related discipline, with at least four years of practical experience in the field of drug discovery in the area of pharmaceutical compounds.

IV. CLAIMS OF THE '381 PATENT

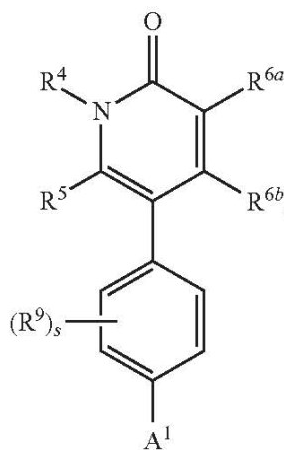
18. The claims of the '381 Patent are as follows.

Claim 1 - A compound having the structure of Formula I:

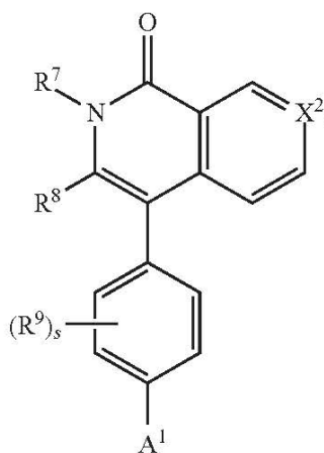


wherein

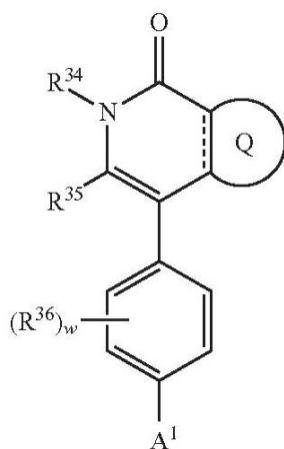
A is:



(Formula IIIb),



(Formula IVa), or



(Formula IX),

wherein

A¹ is a bond between A and L;

s and w are, independently 0, 1, 2, 3, or 4;

R⁴ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl,

R⁵ is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, or optionally substituted C₆-C₁₀ aryl;

R^{6a} is H, halogen, cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

R^{6b} is H, halogen, cyano, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxy, thiol, or optionally substituted amino, or R^{6a} and R^{6b} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl or optionally substituted C_2 - C_9 heteroaryl;

R^7 is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_{10} carbocyclyl;

R^8 is H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_6 - C_{10} aryl;

each R^9 is, independently, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

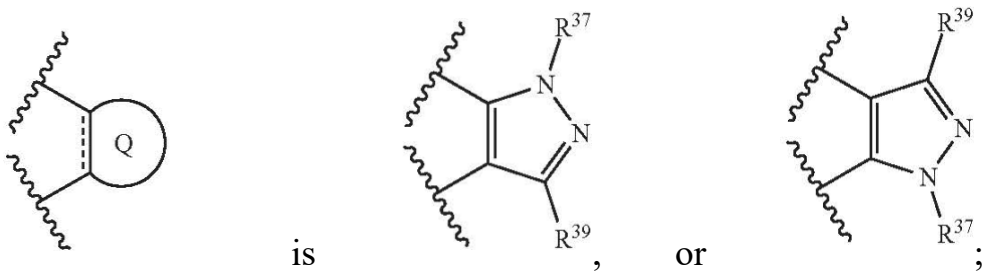
X^2 is N or CR^{10b} ;

R^{10b} is H, halogen, hydroxy, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

R³⁴ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

R³⁵ is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₆ carbocyclyl, or optionally substituted C₆-C₁₀ aryl;

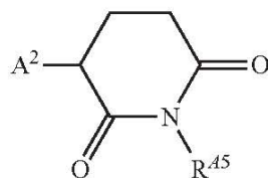
each R³⁶ is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino;



R^{37} is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl; and

R^{39} is H, halogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_6 - C_{10} aryl;

B is:



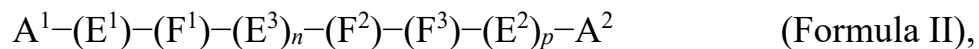
(Formula AA2),

wherein

A^2 is a bond between B and L; and

R^{45} is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl;

L is:



wherein

A^1 is a bond between the linker and A;

A² is a bond between B and the linker;

n is 0 or 1;

p is 0 or 1;

each of E¹ and E² is, independently, O, S, NR^N, optionally substituted C₁₋₁₀ alkylene, optionally substituted C₂₋₁₀ alkenylene, optionally substituted C₂₋₁₀ alkynylene, optionally substituted C_{2-C10} polyethylene glycol, or optionally substituted C₁₋₁₀ heteroalkylene;

E³ is optionally substituted C_{1-C6} alkylene, optionally substituted C_{1-C6} heteroalkylene, O, S, or NR^N;

each R^N is, independently, H, optionally substituted C₁₋₄ alkyl, optionally substituted C₂₋₄ alkenyl, optionally substituted C₂₋₄ alkynyl, optionally substituted C₂₋₆ heterocyclyl, optionally substituted C₆₋₁₂ aryl, or optionally substituted C₁₋₇ heteroalkyl; and

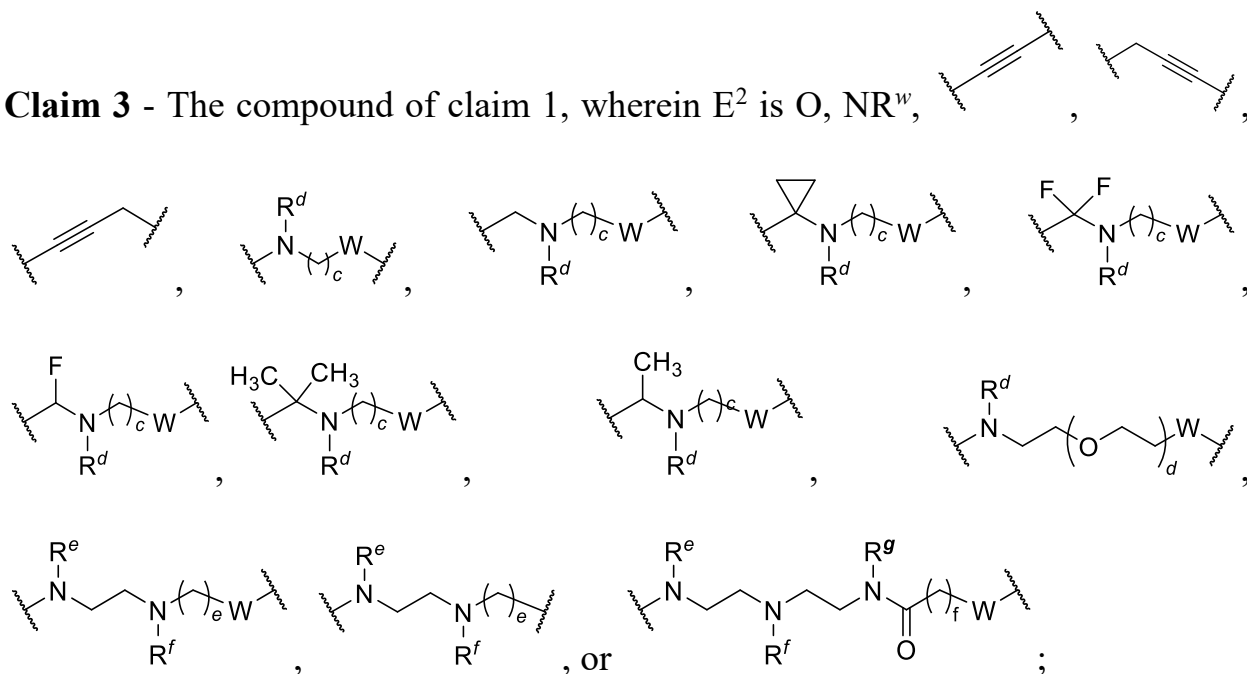
each of F¹, F², and F³ is, independently, optionally substituted C_{3-C10} carbocyclylene, optionally substituted C_{2-C10} heterocyclylene, optionally substituted C_{6-C10} arylene, or optionally substituted C_{2-C9} heteroarylene;

or a pharmaceutically acceptable salt thereof. (Ex.1001,502-503¹).

Claim 2 - The compound of claim 1, wherein E¹ is —CH₂—. (*Id.*).

¹ Citation is to Exhibit page number.

Claim 3 - The compound of claim 1, wherein E² is O, NR^w,



wherein

c is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

d is 0, 1, 2, or 3;

e is 0, 1, 2, 3, 4, 5, or 6;

f is 0, 1, 2, 3, or 4;

R^d is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^e is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^f is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

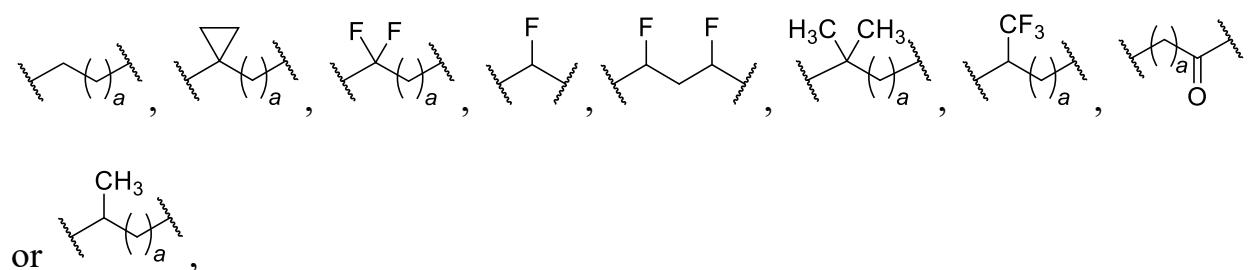
R^g is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl; and

W is O or NR^w, wherein R^w is H or optionally substituted C₁-C₆ alkyl. (*Id.*).

Claim 4 - The compound of claim 3, wherein E² is —NR^N—. (*Id.*).

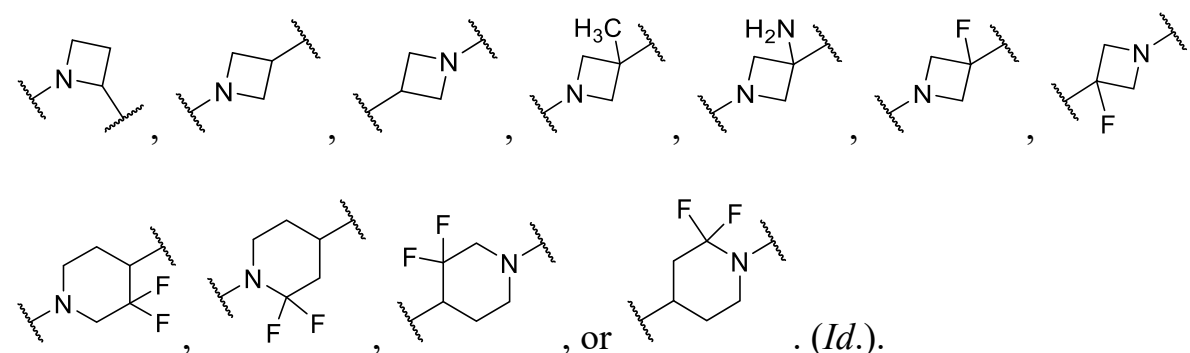
Claim 5 - The compound of claim 4, wherein E² is —NH—. (*Id.*).

Claim 6 - The compound of claim 1, wherein n is 1 and E³ is

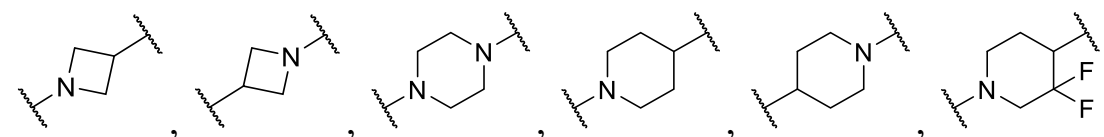


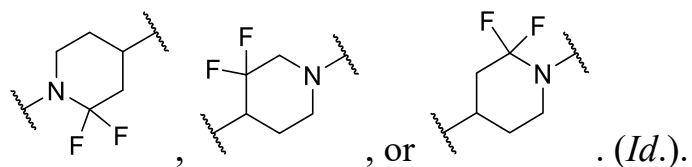
where a is 0, 1, 2, 3, 4, or 5. (*Id.*,503-504).

Claim 7 - The compound of claim 1, wherein F¹ is



Claim 8 - The compound of claim 1, wherein F² is

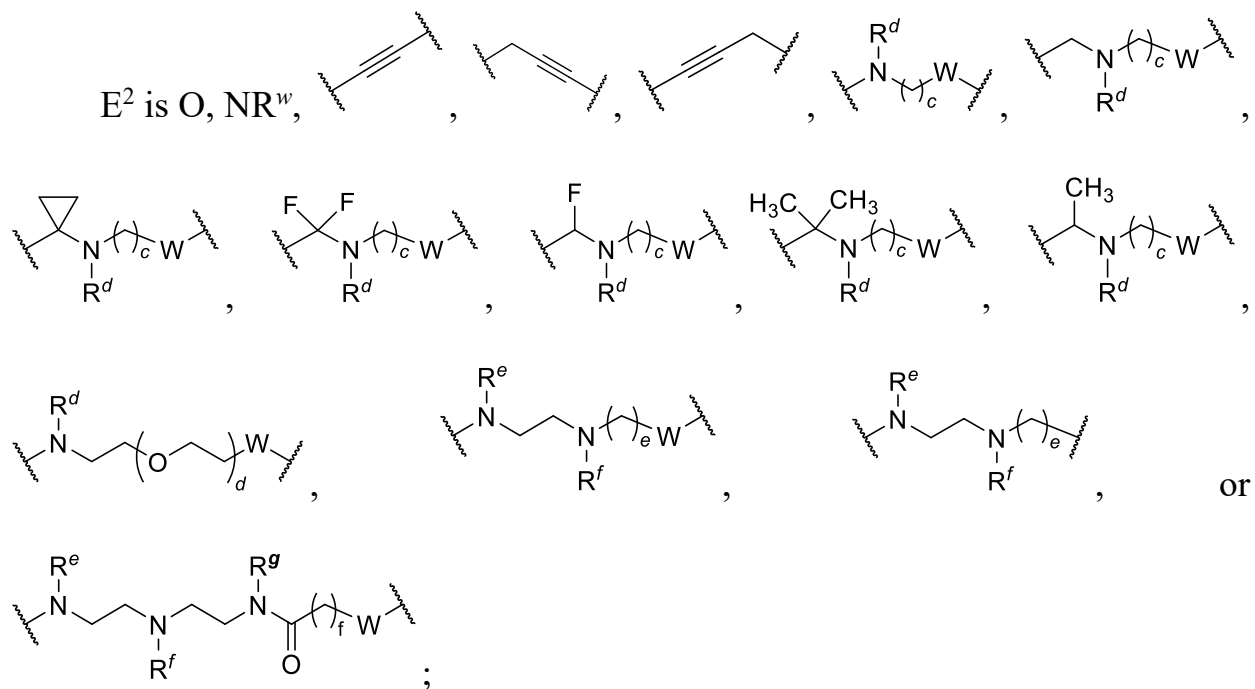




Claim 9 - The compound of claim 1, wherein F³ is optionally substituted C₆-C₁₀ arylene. (Id.).

Claim 10 - The compound of claim 1, wherein:

E¹ is —CH₂—;



wherein

c is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

d is 0, 1, 2, or 3;

e is 0, 1, 2, 3, 4, 5, or 6;

f is 0, 1, 2, 3, or 4;

R^d is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;

R^e is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;

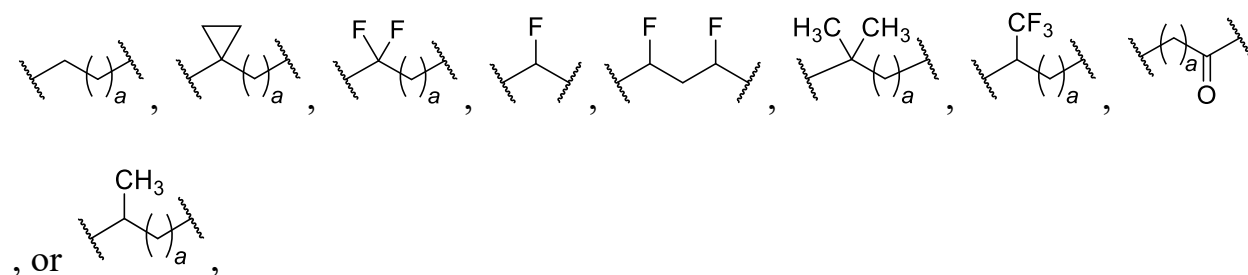
R^f is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;

R^g is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;

W is O or NR^w , wherein R^w is H or optionally substituted C_1 - C_6 alkyl;

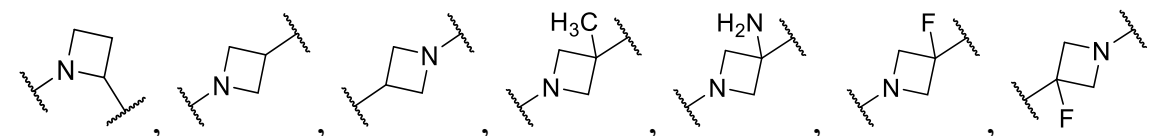
n is 0 or 1;

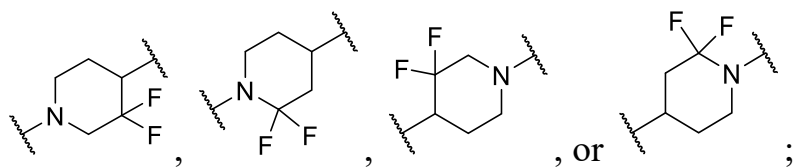
E^3 is



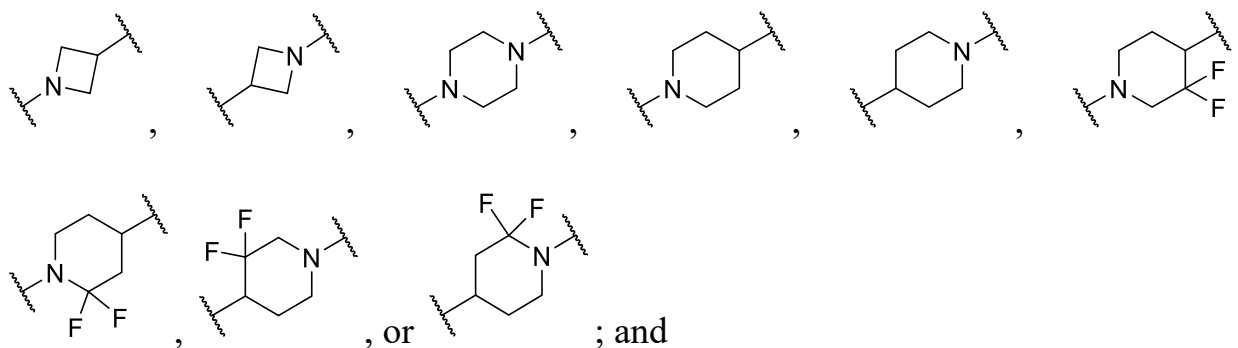
where a is 0, 1, 2, 3, 4, or 5; and

F^1 is





F² is



F³ is optionally substituted C₆-C₁₀ arylene. (*Id.*,504-505).

Claim 11 - The compound of claim 1, wherein p is 1. (*Id.*).

Claim 12 - The compound of claim 10, wherein p is 1. (*Id.*).

V. THE CLAIMS OF THE '381 PATENT INCLUDE MANY STRUCTURES WHICH CANNOT BE MADE OR WOULD NOT BE STABLE

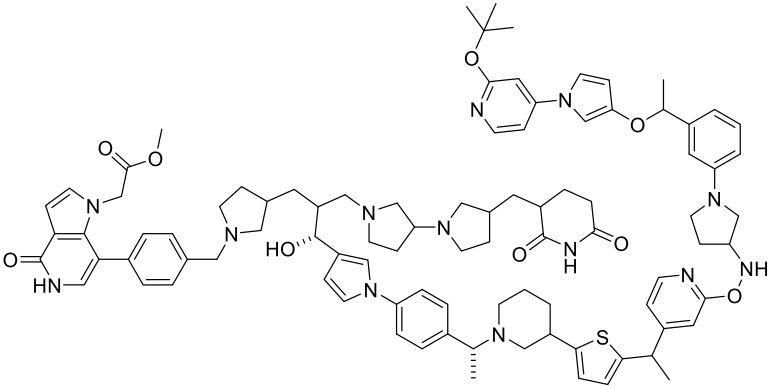
19. I have been asked to consider the scope of compounds covered by the claims of the '381 Patent and compare them to the teachings of the specification as read by a POSA to determine if the claims are enabled. To help visualize the scope of the claims I drew seventy-four compounds which are covered by the claims and considered, based on my expertise in medicinal chemistry, the amount of experimentation to make and use the drawn compounds. These compounds are just

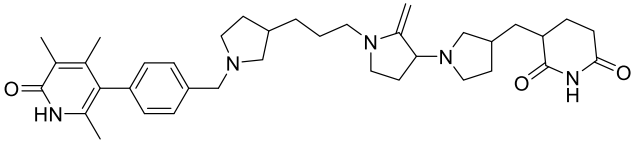
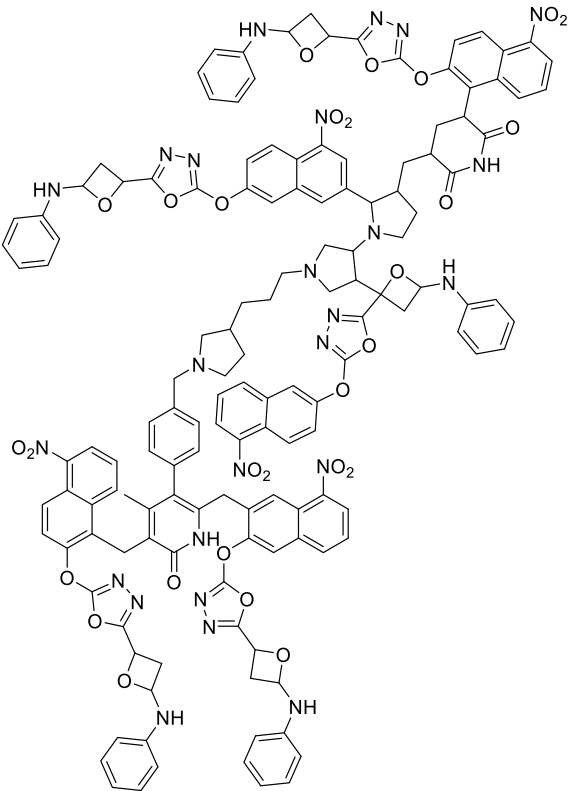
a small example of the vast chemical space covered by the claims and because of the use of the term “optionally substituted” without limitation in every claim there are an infinite number of compounds that a POSA would need to sort through to make and use the claimed invention. In my opinion a POSA would not be able to determine if a compound of interest fell within the claims because the scope is so uncertain because of the use of open-ended optional substituents.

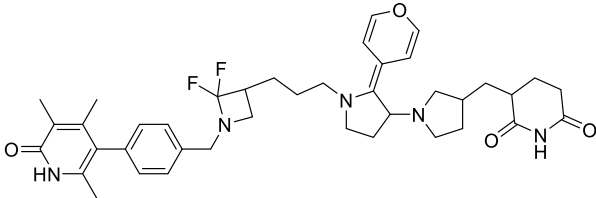
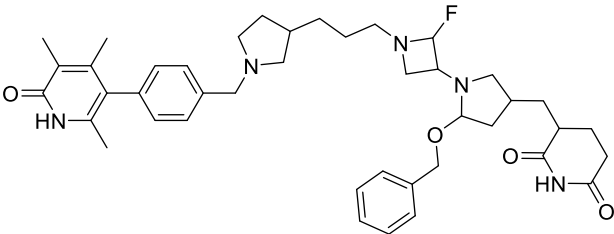
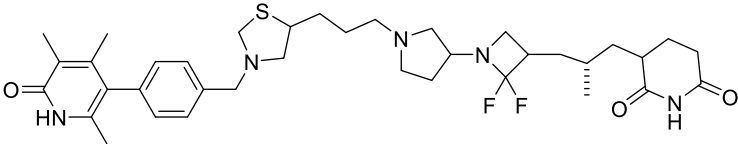
20. The compounds are provided in Table 1 below.

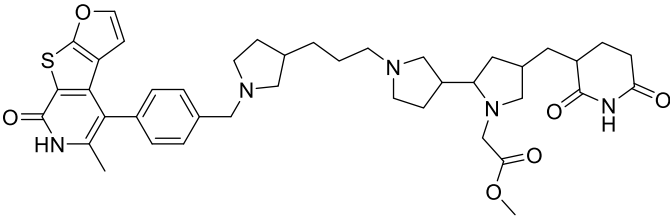
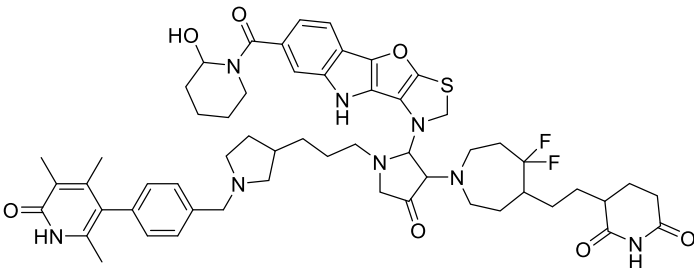
Table 1

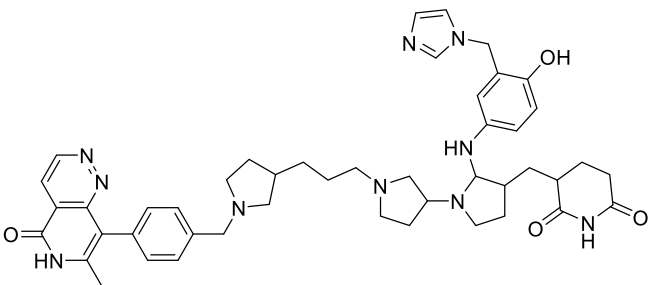
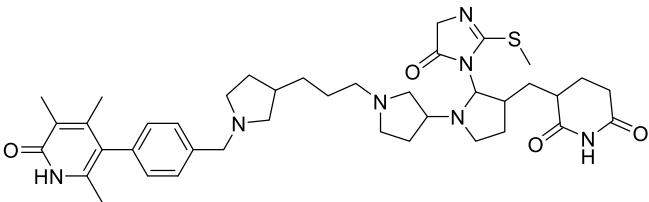
Claimed Formulas	

Examples	Claim # and Remarks
	This very large, highly chiral compound would take excessive experimentation to synthesize. In my opinion it would take at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success. Additionally, in my opinion, the N-O bond may cleave. 1

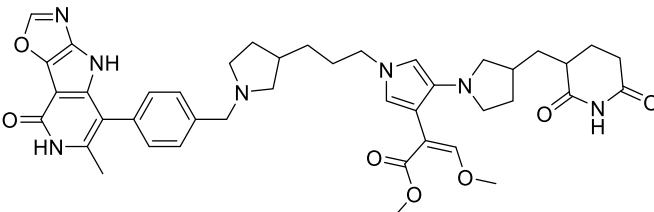
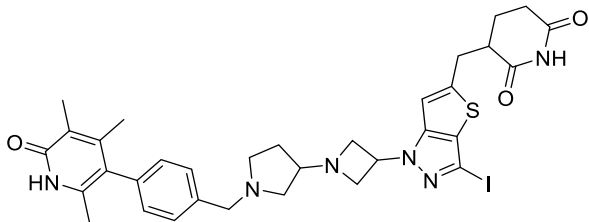
	I would consider this vinyl amine to be unstable/reactive particularly in acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	This very large, highly chiral compound would take excessive experimentation to synthesize. In my opinion it would take at least six months to synthesize and isolate the various chiral isomers of this

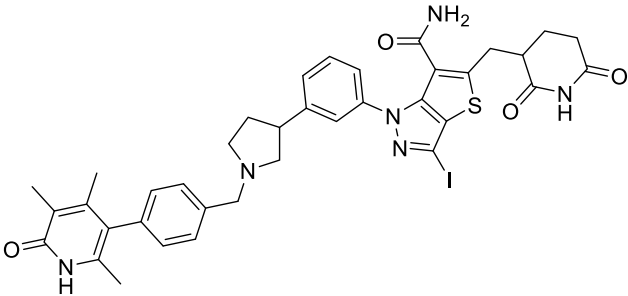
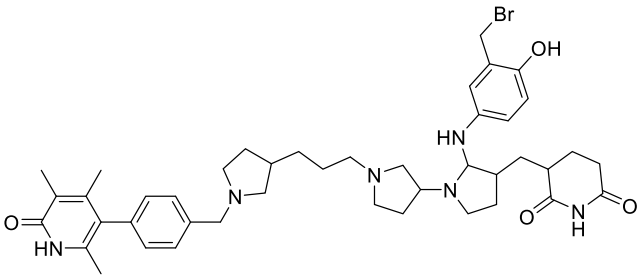
		compound with no guarantee of success.
	1	In my opinion this compound would not be stable <i>in vivo</i> .
	1	In my opinion the hemiaminal in the Linker will break down, particularly in acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	1	The thiazolidine is prone to oxidation and/or cleavage and would not be stable <i>in vivo</i> .

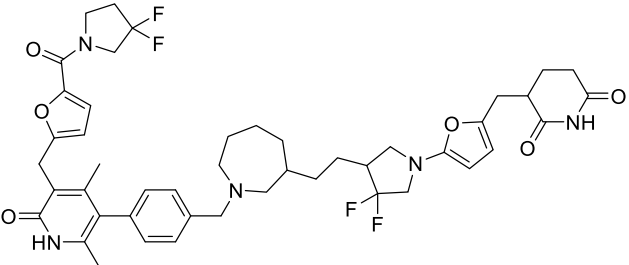
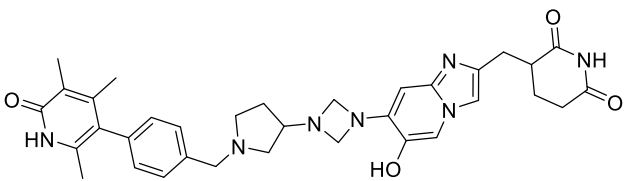
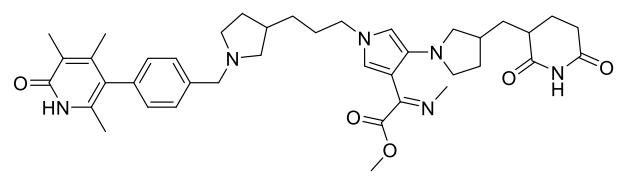
	1 There is no structure activity relationship (SAR) in the application to support the use of tricyclic BRD9 ligands. Additionally, in my opinion the ester would be unstable <i>in vivo</i>.
	1 In my opinion this compound is highly unstable and could break down at several sites including at the aminal, hemiaminal, and antiaromatic ring. This compound would be exceedingly difficult or impossible

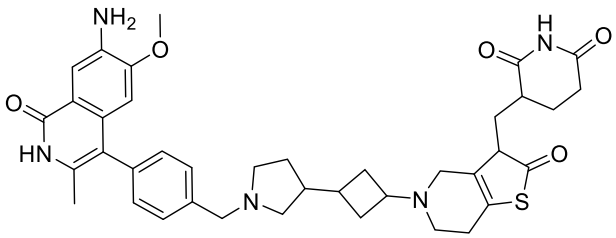
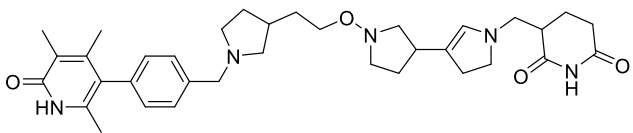
		to synthesize and isolate.
	1	In my opinion this compound is unstable at least because of the inclusion of a reactive quinone-like moiety and an aminal moiety. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	1	In my opinion this compound is unstable and will release a toxophore². This compound is not appropriate for

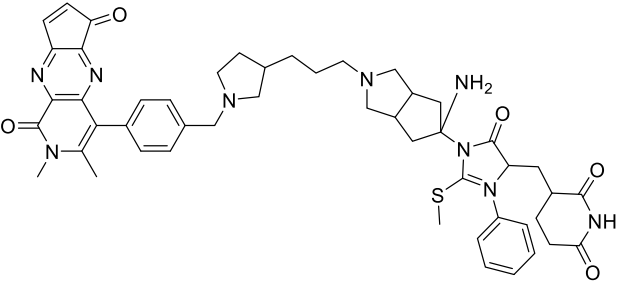
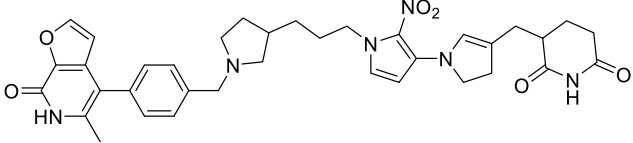
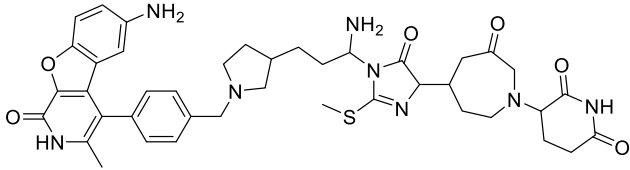
² A toxophore is a chemical group that is cause a toxic effect *in vivo*.

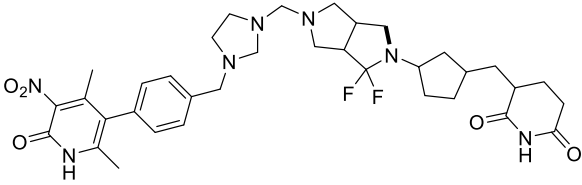
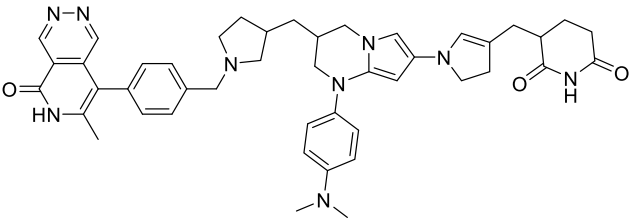
		administration to a human.
	1	This compound includes a toxophore, <i>in vivo</i> cleavable ester and new tricyclic BRD9 ligand. Success is unlikely and this compound is not appropriate for administration to a human.
	1	The iodo-heteroaryl moiety is subject to nucleophilic addition which would require excess experimentation to make and use the compound.

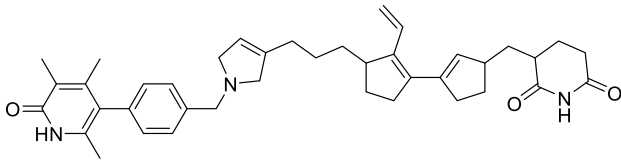
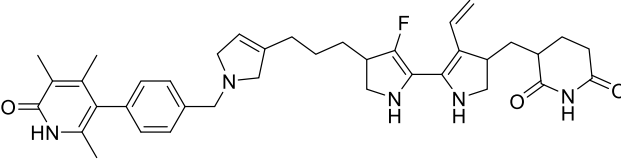
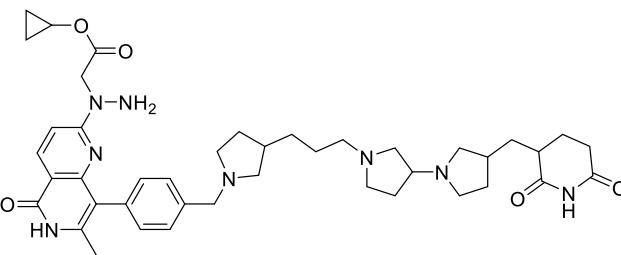
	1	The iodo-heteroaryl moiety is subject to nucleophilic addition which would require excess experimentation to make and use the compound.
	2	In my opinion this compound is unstable at least because of the inclusion of a reactive quinone-like moiety and an aминаl moiety. This compound would be exceedingly difficult or impossible to synthesize and isolate.

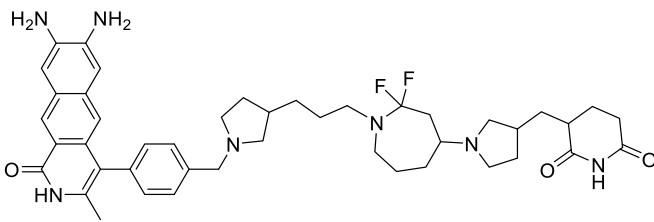
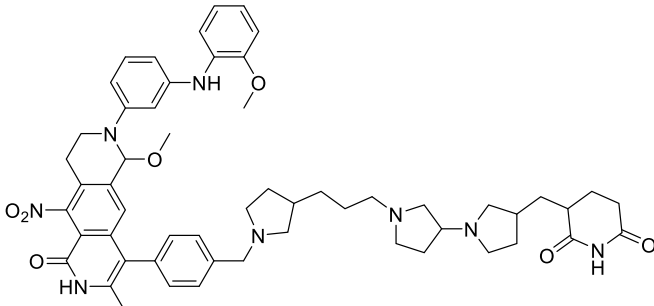
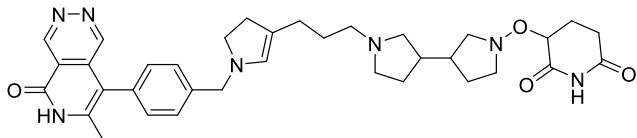
	2	In my opinion the furan moiety is subject to oxidation to a dione and is likely reactive, with little or no possibility of success.
	2	In my opinion this compound would be reactive and not useful as a therapeutic agent.
	2	This compound includes a toxophore. This compound is not appropriate for administration to a human.

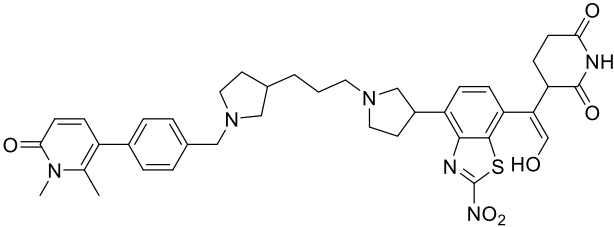
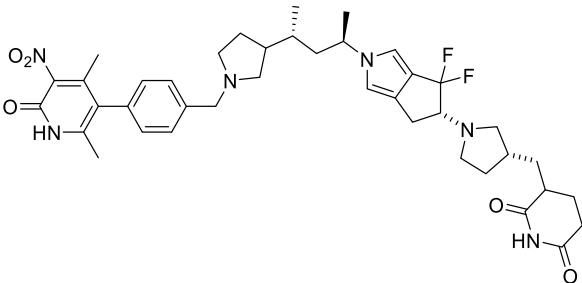
	2	In my opinion this compound would undergo oxidative and rearrangement reactions, and so it would not be suitable for <i>in vivo</i> administration.
	2	In my opinion the N-O bond is prone to oxidative cleavage, and so it would not be suitable for <i>in vivo</i> administration. Moreover, the vinyl amine will be unstable.

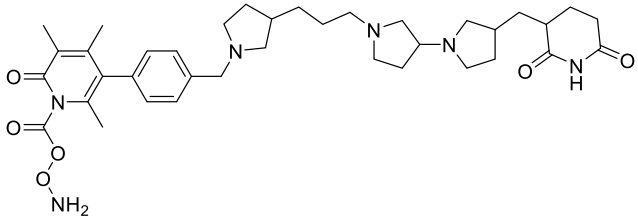
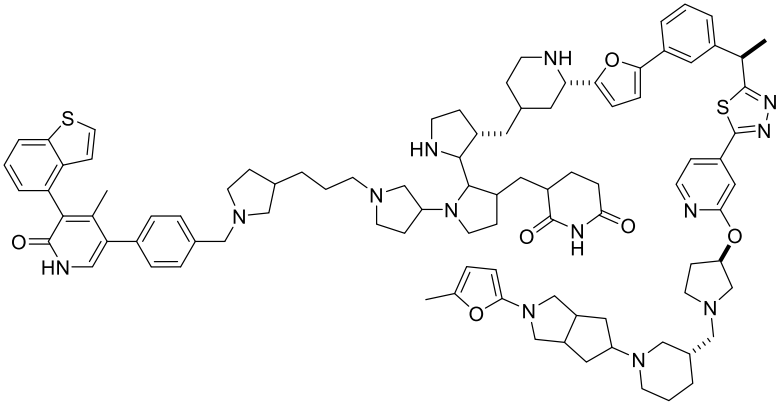
	2	In my opinion the F³ moiety in this compound is unstable and would require excess experimentation to make and use the molecule, if at all possible.
	2	I would consider this vinyl amine heterocycle to be unstable/reactive particularly in acidic media.
	2	In my opinion the F² moiety in this compound is unstable. This compound would be exceedingly

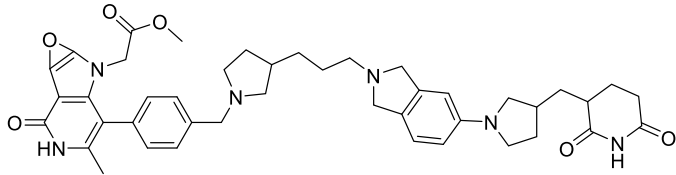
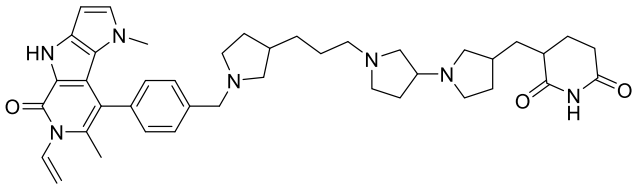
		difficult or impossible to synthesize and isolate.
	2	In my opinion the aminal in the Linker is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	2	I would consider this vinyl amine heterocycle to be unstable/reactive particularly in acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.

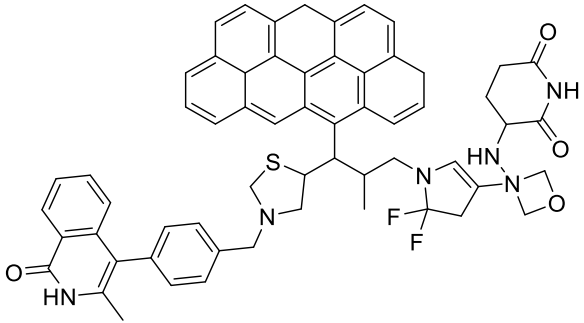
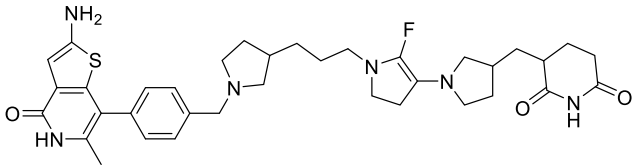
	2	In my opinion the poly-olefin is highly reactive and inappropriate for use as a BRD9 degrader.
	2	In my opinion the poly-olefin is highly reactive and inappropriate for use as a BRD9 degrader.
	2	In my opinion the amino pyridine is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.

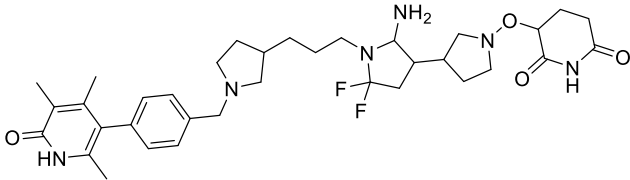
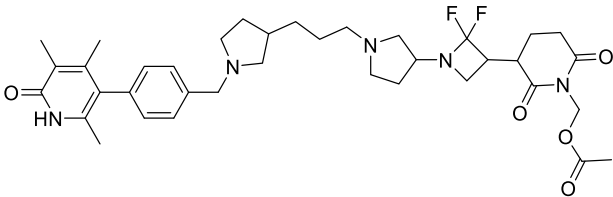
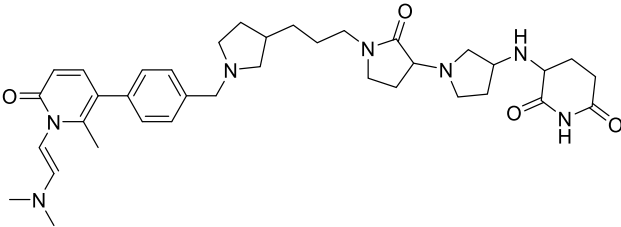
	2	There is no SAR in the application to support the use of tricyclic BRD9 ligands or 7-membered heterocyclic Linkers. Success is doubtful.
	2	In my opinion the the heavily electron rich BRD9 ligand is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	2	In my opinion the N-O bond may cleave and this compound is

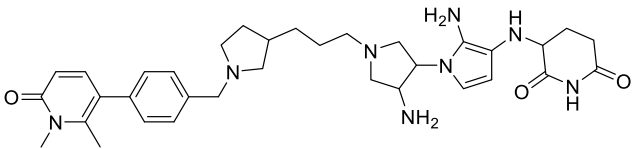
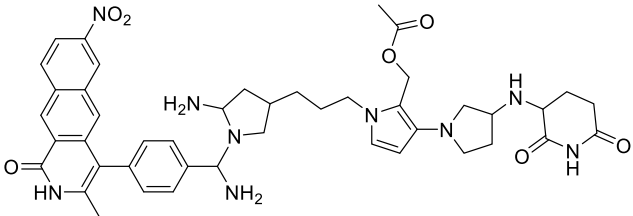
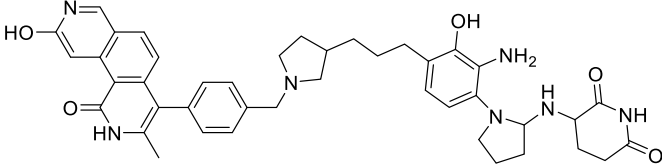
		inappropriate for <i>in vivo</i> administration. Furthermore, the vinyl amine is unstable.
	2	In my opinion the vinylogous alcohol E² group is unstable/reactive and this compound is inappropriate for <i>in vivo</i> administration.
	2	This compound includes a chiral Linker that would be difficult to synthesize in various chiral configurations.

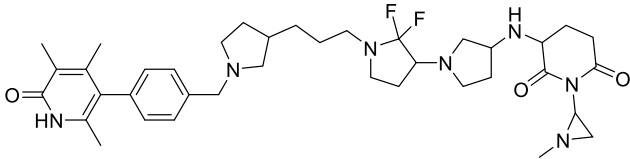
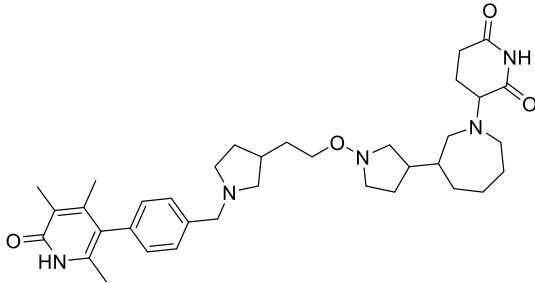
	2	In my opinion the BRD9 Ligand substituent is unstable.
	2	This very large, highly chiral compound would take excessive experimentation to synthesize. In my opinion it would take at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success.

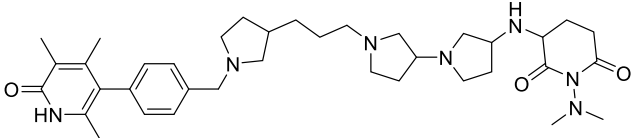
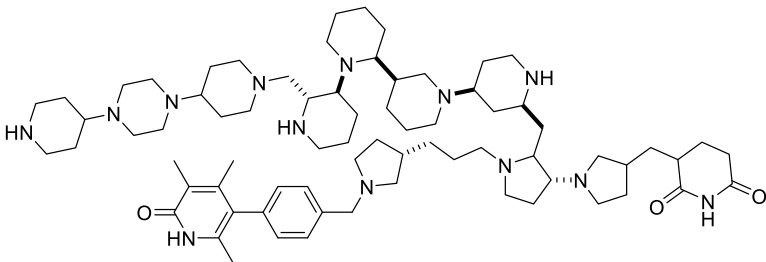
		and reactive. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	2	In my opinion the BRD9 ligand portion is unstable because of the highly strained epoxide as well as cleavable ester. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	2	I would consider this vinyl amine to be unstable, particularly in acidic media.

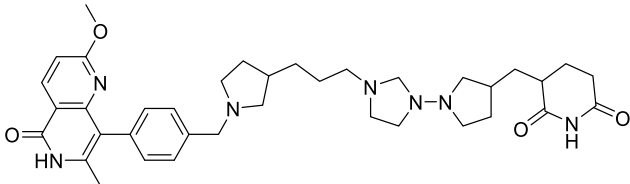
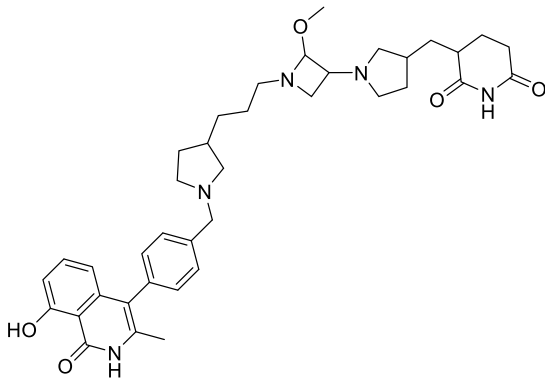
	3 The thiazolidine is prone to oxidation and/or cleavage and in my opinion the N-N bond is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	3 I would consider this vinyl amine heterocycle to be unstable/reactive particularly in acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.

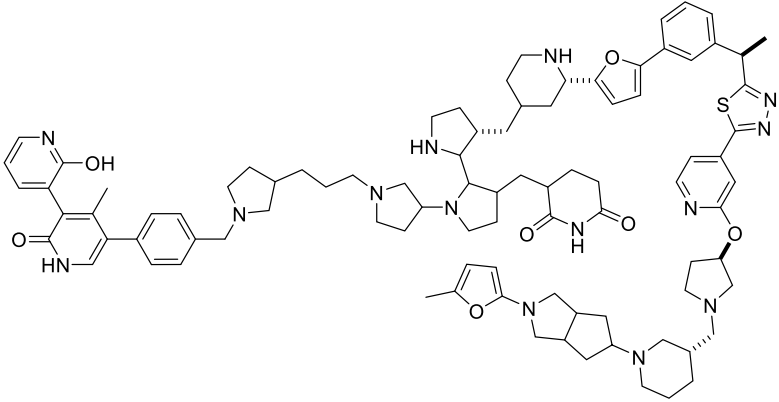
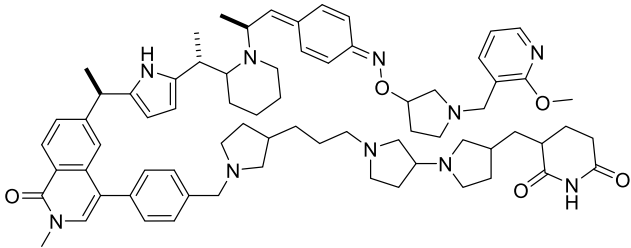
	3	In my opinion the N-O bond is prone to oxidative cleavage. This compound would not be stable <i>in vivo</i>. Furthermore the amination is unstable.
	3	In my opinion the ester is unstable <i>in vivo</i>.
	3	I would consider this vinyl amine to be unstable particularly in acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.

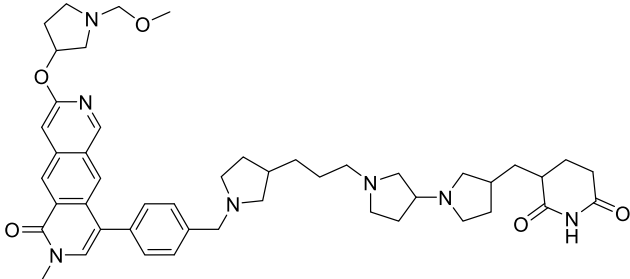
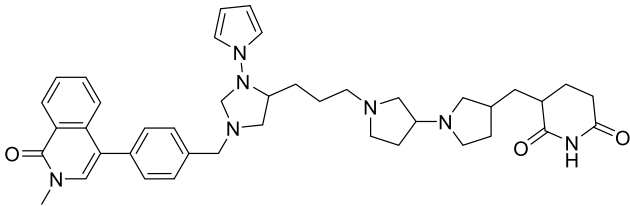
	4	In my opinion the amino pyrrole Linker is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	4	In my opinion the aiminal is unstable. Additionally, there is no SAR in the application to support the use of tricyclic BRD9 ligands, nitro functional groups, or esters substituents. Success is doubtful.
	4	In my opinion this compound is reactive

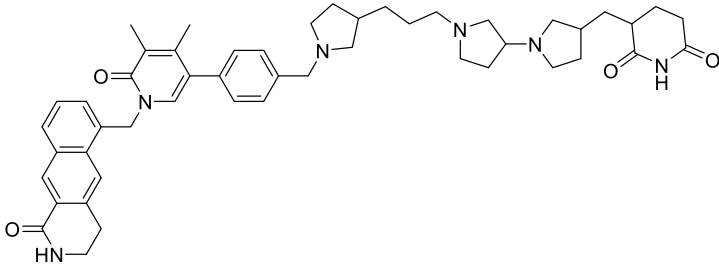
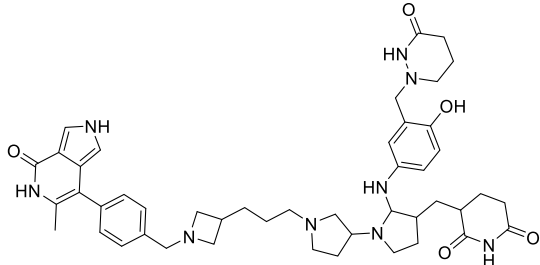
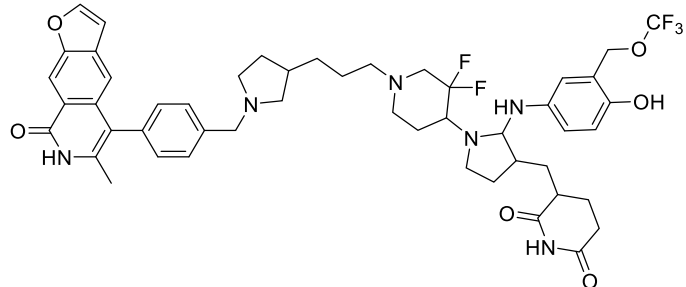
		acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	5	In my opinion the aminal in the glutarimide will break down, particularly in acidic media. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	5	In my opinion the N-O bond is prone to oxidative cleavage. This compound is not appropriate for <i>in vivo</i> administration.

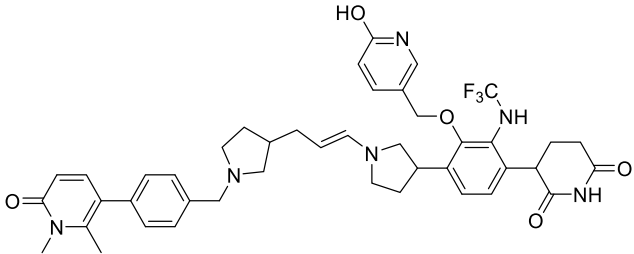
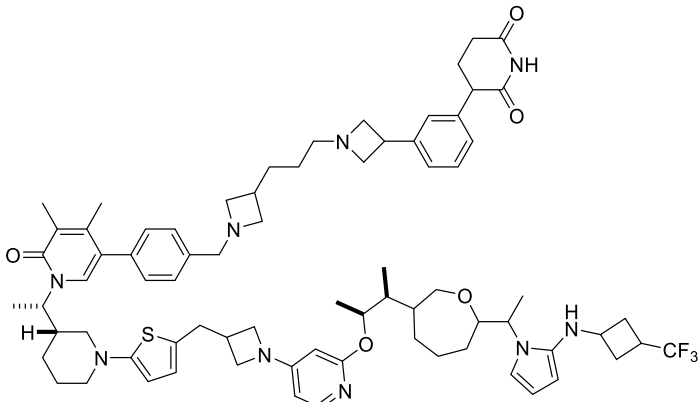
	In my opinion the N-N bond is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	This very large, highly chiral compound would take excessive experimentation to synthesize. In my opinion it would take at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success.

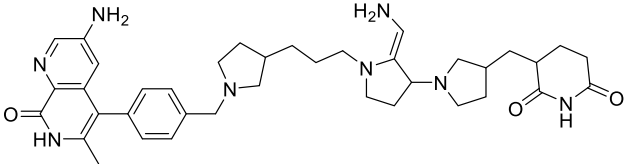
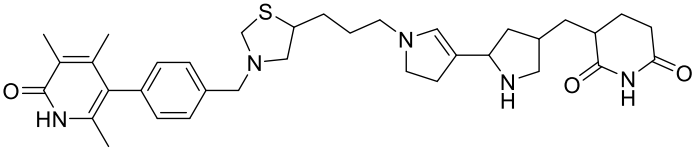
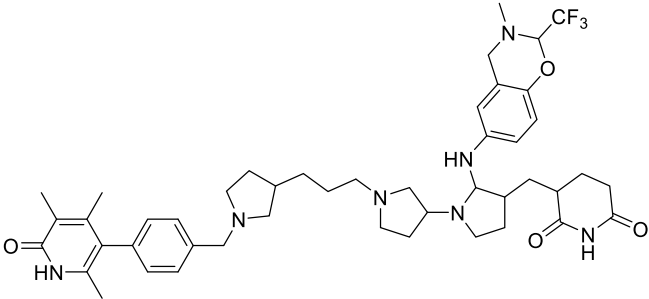
		exceedingly difficult to synthesize.
	6	In my opinion the N-N bond is unstable. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	6	In my opinion the hemiaminal in the Linker will break down, particularly in acidic media. This compound is not appropriate for <i>in vivo</i> administration.

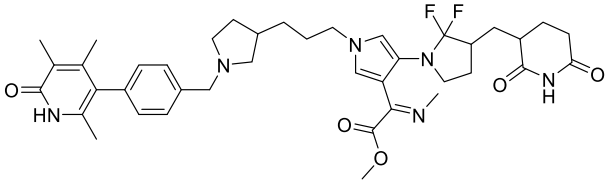
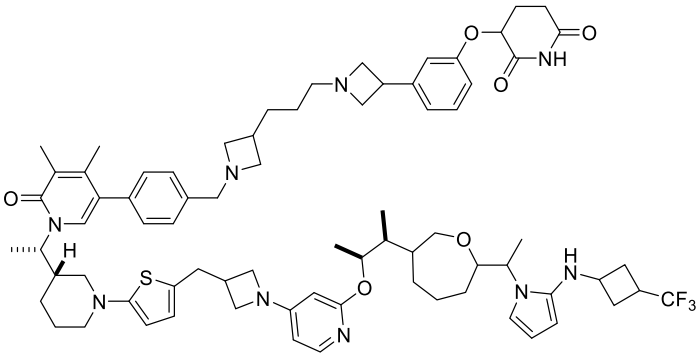
	This very large, highly chiral compound would take excessive experimentation to synthesize. In my 6 opinion it would take at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success.
	This very large, highly chiral compound would take excessive 6 experimentation to synthesize. In my opinion it would take

		at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success.
	6	In my opinion the hemiaminal substituent in the BRD9 ligand is unstable.
	6	In my opinion the N-N pyrrole is unstable and will release a toxophore. This compound is not appropriate for administration to a human.

	6	In my opinion the BRD9 optional substitution is subject to oxidative reactivity.
	7	In my opinion this compound includes several unstable functional groups. This compound would be exceedingly difficult or impossible to synthesize and isolate.
	8	This compound includes a reactive quinone like moiety. This compound would be exceedingly difficult or impossible

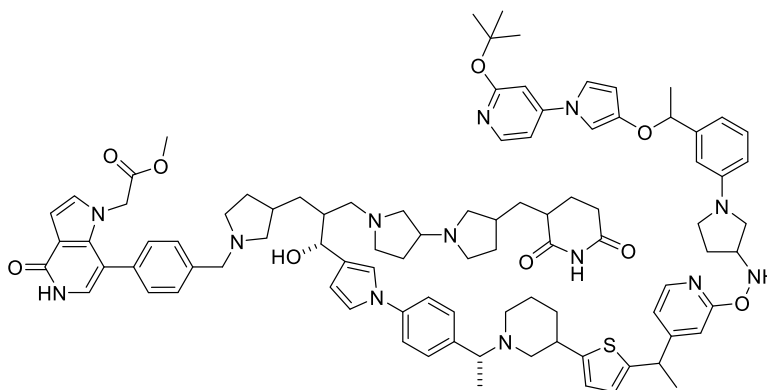
		to synthesize and isolate.
	9	This compound is subject to cleavage in the Linker region.
	10	This very large, highly chiral compound would take excessive experimentation to synthesize. In my opinion it would take at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success.

	11	In my opinion this vinyl amine is unstable, particularly in acidic media, and it will cleave during synthesis.
	11	The thiazolidine is prone to oxidation and/or cleavage and the vinyl amine is unstable. This compound would not be stable <i>in vivo</i>.
	11	In my opinion the amina and/or hemiaminal in the Linker will break down, particularly in acidic media.

	11	This compound includes a toxophore. This compound is not appropriate for administration to a human.
	12	This very large, highly chiral compound would take excessive experimentation to synthesize. In my opinion it would take at least six months to synthesize and isolate the various chiral isomers of this compound with no guarantee of success.

21. For each compound in the Table above I provide a brief explanation of why it would require undue experimentation for a POSA to make and/or use the claimed compound. There are points of serious uncertainty in the vast scope of the claims and this uncertainty is further exacerbated by the inclusion of an infinite loop in the definition of “optionally substituted.” A POSA could draw any number of whimsical compounds that could not be made and/or would not have stability.

22. Several of my structures require multiple layers of optional substituents for construction to demonstrate the large size of compounds that the claims cover. For example, the first structure in Table 1 uses the infinite loop definition on one substituent in the Linker region.



23. A POSA based on the teachings of the application would not know if this compound would be a BRD9 degrader *in vivo* based on the massive departure from the SAR described in the specification. The compound is likely inactive because of the steric bulk on the Linker, but to exclude the possibility of activity the compound would have to be synthesized which would be a very difficult undertaking

because of its size, number of chiral centers, and inclusion of an NH-O motif. A POSA would have to conduct an undue number of experiments to determine the SAR for compounds of this size with possible modifications at nearly every position. No data was provided in the '381 specification that would allow me to answer this question.

VI. LEGAL STANDARDS

A. Burden of Proof

24. I understand from counsel that a post-grant review may be instituted if Petitioner shows that it is more likely than not that at least one claim of the challenged patent is unpatentable. I understand Petitioner bears the ultimate burden of proving that the challenged claims are unpatentable by a preponderance of the evidence which means that there is a greater than 50% chance that the challenged claim is invalid.

B. The Enablement Requirement

25. I am told that 35 U.S.C. §112(a) says:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

26. I understand from counsel that the enablement requirement of 35 U.S.C. §112(a) mandates that the specification of a patent must teach the POSA how to make and use the full scope of the claimed subject matter without undue experimentation. I understand that whether experimentation is undue is a conclusion reached by weighing many factual considerations, including (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. I understand that these factors are illustrative and not mandatory, and that some factors may be more important than others depending on the circumstances.

27. I understand from counsel that to meet the how-to-use requirement, the specification must establish that the claimed invention achieves its intended purpose. In this case that would mean that the compounds covering the full scope of the '381 claims can degrade BRD9 in a therapeutically useful manner on administration to a human.

28. I am also told that in the unpredictable arts, especially those that involve new and incompletely understood technology, the specification is required to give more guidance to one of ordinary skill in the art to enable the full scope of the claims. In my opinion the field of heterobifunctional compounds generally and

therapeutic protein degradation specifically is a difficult field with many new and not completely understood complexities.

C. Indefiniteness of Patent Claims

29. I am told that 35 U.S.C. §112(b) states:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

30. I have also been informed that the claims of a patent must particularly point out the claimed subject matter so that the metes and bounds, or the scope, is clearly defined to the POSA. I understand from counsel that claims are in compliance with §112(b) if they adequately inform a POSA of the scope of the invention with reasonable certainty.

31. I have been told that in certain circumstances, a claim is indefinite if it is so expansive that the POSA cannot determine the metes and bounds of the claimed invention. I understand from counsel that sometimes a claim defines a chemical compound using one or more “Markush” groups, which are claims that recite a list of alternative useable members, and as is the case here, a chemical structure with substituents defined by variables. Where a Markush claim encompasses a massive number of distinct alternative members, I understand that the claim is indefinite under § 112(b) if a POSA cannot determine its metes and

bounds due to an inability to identify all of the compounds defined by the Markush group(s).

VII. CONCLUSIONS

32. Based on my review of the matters described herein and based on my training and experience managing scientist in the field of pharmaceutical drug discovery, including heterobifunctional therapeutics, it is my opinion and conclusion that all of the claims of the '381 Patent are invalid under 35 U.S.C. §112(a) and §112(b).

33. In accordance with 37 C.F.R. 1.68, I have been warned that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. 1001). All statements made of my own knowledge are true and all statements made on information and belief are believed to be true.

A handwritten signature in black ink, appearing to read 'Kevin Tyler Sprott', written over a horizontal line.

Kevin Tyler Sprott, Ph.D.

Oct. 19 2023

Date

ATTACHMENT 1

Kevin Tyler Sprott, Ph.D.

Executive Summary

An entrepreneurial and energetic scientific drug hunter with a proven history of working collaboratively with inter-disciplinary scientists, business partners and investors to successfully advance companies and small molecule drug discovery programs from the earliest stages through to human clinical development, providing maximum value for patients and shareholders. A people-first leader with a track record of building highly-engaged and high-performing teams.

Led or contributed to 10 development candidates and clinical-stage assets across 6 companies

- ▣ Millennium (acquired by Takeda 2008, \$8.8B); Medicines: MLN-4924, MLN-6095, MLN-0905
- ▣ Ironwood Pharma (IPO 2010); Medicines: IW-6118, IW-7229, IW-1221
- ▣ Verastem Oncology (IPO 2012); Medicines: VS-4718, VS-6063
- ▣ Syros Pharmaceuticals (IPO 2016); Medicines: SY-1365, SY-5609
- ▣ SMOC Therapeutics (Acquired 2020, Ventus Tx, \$60M Series A)
- ▣ Stablix, Inc (\$78M Series A, April 2021; Research Partnership, April 2023)

Professional Experience

Stablix Inc., NY NY; Boston MA

2021-2023

Stablix, Inc was founded in 2021 from Columbia Medical School from the lab of Henry Colecraft, focused on leading a novel therapeutic modality of Targeted Protein Stabilization

Founder, Chief Operating Officer

Prepared for and drove discussions with 30+ potential investors, culminating in a \$78M Series A.

Drove Business Development relationships, culminating in 4-year Research Partnership in April 2023.

As a founder and first employee at Stablix, responsible for “standing up” the company including scientific strategy, operational build-out, full G&A functions and working with the board to set and execute on initial corporate and research strategies.

Summary of active areas and key responsibilities:

- Corporate and Scientific Strategy: LRP development/alignment
- Investor Relations: capital raise, existing/future investor communication
- Business Development: strategy and execution
- Corporate Finance: planning, budgeting, reforecasting, 409a eval, BoD reporting
- Human Resources: organizational design & staffing plans, comprehensive compensation and equity programs, multistate benefits plans, federal & multi-state compliance, hiring, internal HR
- Alliance and Program Management: internal and external program governance
- Corporate Legal: contracts, business deals, BoD resolutions
- PR and Media: press releases, website development, media
- Research Informatics: Database management systems to capture/utilize data
- Facilities and Real Estate: secure leases maintain office, build out and maintain labs

Highlights include:

- Raised \$78M Series A (Versant, NEA, Euclidean, Cormorant, Alexandria)
- Secured multi-target discovery partnership with publicly-traded \$50+B pharma partner. Significant payouts up-front and on early research milestones, with substantial downstream payouts as programs mature.
- Met Tranche 1 goals in 7 months with \$6M leading to release of Tranche 2; hired CEO, CSO, expand staff and footprint
- Built and maintained Long Range Plans, in close contact with BoD and SAB to align on corporate and research strategy
- Built/maintained operational capabilities in IT, IP, legal, HR to enable a stable, efficient, scalable company
- Identified and built lab/office sites in both East River ARE (NY) and Fenway (MA)
- Built a highly competent, fully engaged team of ~30 people (27 in research, 3 in G&A)
- Stablix Scientific accomplishments under my leadership:
 - Established platform, enabling DUB-target pairing, identification of non-inhibitory chemical matter on key DUBs which enables broad efforts in drug discovery
 - Established cellular POC that exceeds SOC in clinically relevant cell lines

- Established world-wide research capabilities, building relationships and partnering with dozens of CROs to support a dynamic research strategy
- Initiated ~5 discovery projects enabled by chemical matter on DUB and target side

Tesova Drug Discovery Consulting, LLC

2019-present

Highlights include:

- Inception, early-stage research strategy and execution, culminating in the launch of Avilar Therapeutics with RA Capital, \$60M Series A targeting extracellular protein degradation
- Diligence and research support leading to Ipsen exercise option to acquire world-wide rights to investigational ERK inhibitor discovered by AGV Discovery
- Contributed to and helped guide decision of early-stage diligence deals with a number of VCs

SMOC Therapeutics, Natick MA

2018-2019

SMOC Tx, a NewCo founded in 2018 from Harvard Medical School, Boston Childrens Hospital, Yale and the Howard Hughes Medical Institute, focused on small-molecule therapeutics targeting innate immune pathways

SMOC Tx was acquired by Ventus Therapeutics and serves as the basis for the discovery engine

- \$60M Series A, \$100M Series B
- Multiple large pharma partnerships

Senior Vice President (de-facto CEO/CSO), Board Director

Hired at company inception, built the foundation of internal and external research as well as all business mechanisms. Responsible for scientific and business strategies, setting corporate goals, planning and execution, reporting to Board of Directors

Highlights include:

- Led scientific strategy and operations resulting in hit chemical matter on 3 early-stage drug discovery programs
- Presented to and ran diligence for 40+ venture capital and pharma business development groups in preparation for future financing, ultimately resulting in acquisition

- Recruited and hired 4 FTE for research in incubator space, multiple global CROs to support external research
- Recruited and hired 3 additional scientific founders, 4 SAB members and many consultants to support a lean internal organization with aggressive approaches to achieve chemical, biophysical and cellular POC

Syros Pharmaceuticals, Cambridge MA

2013-2017

Syros is a publicly traded biotech company developing novel drugs that target gene control mechanisms

Senior Director, Chemistry and Preclinical Development

Development Project Leader, SY-1365

Hired at company inception and as an initial member of the management team, helped build the foundation of research and business at Syros, worked closely with executive management team, internal and external scientists, legal, business development and finance to initiate and advance science and build a forward-integrated biotech company

Highlights include:

- Development Lead, SY-1365 Project (NCT03134638)
 - Led multi-disciplinary team including preclinical/non-clinical, translational medicine, clinical, business development, communications, regulatory, commercial, finance, IP and CMC functions through SY-1365 IND filing and through current Phase 1 dose-escalation safety study in patients with advanced solid tumors
- Project Leader, CDK7 Discovery Project
 - Led multi-disciplinary internal and external research teams to discovery of SY-1365, a small-molecule CDK7 inhibitor for treatment of cancer. SY-1365 was Syros' first internally discovered development candidate
 - Initiated and supported back-up program resulting in orally available SY-5609 (NCT04247126)
- Established, alongside head of biology, physical and virtual drug discovery operation. Capabilities in chemistry, biology, enzymology, biophysics, DMPK, pharmacology and crystallography were established world-wide through careful partner analysis, selection and execution
- Identified, hired and co-managed scientific staff of 30+ FTEs and FFS organizations to execute multiple discovery projects

- Annual discovery budget of approximately \$8-15 Million
- Member of early management team and scientific leadership teams, responsible for shaping corporate and scientific strategy, making investment and programmatic decisions across the portfolio

Verastem, Inc., Cambridge MA

2011-2013

Verastem is a commercial-stage, publicly traded pharmaceutical company developing novel drugs that target tumor microenvironment and malignant B-cells

Senior Director, Chemistry

As a founding scientist and member of the management team, helped build the foundation of research at Verastem, working closely with SAB members to gauge programs that best positioned Verastem to bring novel drug candidates to human clinical development and market.

Highlights include:

- Established virtual and internal chemistry and biology scientific operations in China, Canada and U.S.:
 - Involved with identification, hiring and managing scientific staff of 20 FTEs to execute on multiple projects
 - Annual budget of approximately \$2.2 Million
- Key contributor and project leader to Verastem's research and development portfolio:

Focal adhesion kinase inhibitor project (NCT0265172, NCT03287271)

- Actively involved with in-licensing 4 novel preclinical and clinical stage FAK inhibitors, deals ranging in committed capital to \$3 million dollars including milestones
- Discovered 3 novel series of FAK inhibitors, culminating in delivery of DC VS-4718 (NCT0265172)
- Provided diligence on acquisition of Phase 2 FAK Inhibitor VS-6063 (formerly PF-04554878, NCT03287271) PI3K/mTOR project
- Using high-throughput screens, identified PI3K/mTOR as key pathway for cancer stem cell survival
- Actively involved with in-licensing a Phase-1-ready

PI3K/mTOR inhibitor

- Established and managed assays at CROs to evaluate product versus competitor molecules Salinomycin project

- Collaborated with V.P. of Business Development to structure and close non-dilutive \$1 million transaction with Eisai
 - Managed Salinomycin project with President of Eisai global process chemistry
 - Designed and synthesized novel, active, analogs of Salinomycin
- Phenotypic research projects
- Successfully identified attractive drug-like hits from 320,000-compound high-throughput screen
 - Prioritized and led 6 projects with novel chemical matter that target cancer stem cells ▪
- Head of Internal Intellectual Property:
 - Managed external attorneys to support Verastem IP filings, licensing transactions, and budget; managed office actions with external attorneys for a portfolio of over 22 patent families
 - Managed internal teams and external attorneys to evaluate IP position for potential in-licensing opportunities
 - Annual IP budget of approximately \$750,000
 - Contributed to writing disclaimers for securities filings made to SEC in connection with \$55 million IPO
 - Active member of due diligence team, evaluated in-licensing opportunities, pre-clinical stage to Phase III

**Ironwood Pharmaceuticals (formerly Microbia, currently Cycleron),
Cambridge MA 2006-2011**

Ironwood is a commercial stage, publicly traded pharmaceutical company dedicated to creating, developing, and commercializing innovative human medicines.

Principal Investigator, Medicinal Chemistry/Program Management

As a member of both medicinal chemistry and program management groups, collaborated with highly cross-functional teams, successfully initiated and drove small molecule from early discovery to clinical development

Highlights include:

- Medicinal chemistry lead: FAAH inhibitor program, pain and inflammation
 - Culminated in the discovery of development candidates IW-6118 (NCT01107236) and IW-7229
- Medicinal chemistry co-lead: GPCR antagonist program, asthma

- Culminated in the discovery and selection of development candidate IW-1221
- Identified and proposed, and ultimately gained CSO-sponsored approval, for numerous discovery projects – included building scientific, clinical, and commercial rationale, staffing and funding plans, and operational goals.
- Team project lead: Cannabinoid receptor 2 agonist program, pain and inflammation
 - Led a group of ~25 interdisciplinary scientists
 - Discovered 2 novel chemical series demonstrating strong in-vivo efficacy following oral dosing
 - Project annual budget approximately \$5-7 million
- Team project lead: enzyme inhibitor program, multiple sclerosis o Led a group of ~8 interdisciplinary scientists
 - Identified novel inhibitors that demonstrated in-vivo proof-of-concept
 - Project annual budget \$2 Million
- Chair: small molecule programs advisory committee
 - Appointed by CSO to identify, monitor and prioritize early-stage opportunities in drug discovery

Millennium Pharmaceuticals, Cambridge MA

2003-2006

Millennium is currently the Takeda Oncology Company

Scientist, Inflammation and Oncology Medicinal Chemistry

As a member of the medicinal chemistry team, worked with large cross-functional groups that successfully identified 3 assets selected for clinical development

Highlights include:

- Medicinal chemistry lead: CCR2 antagonist program, pain and inflammation
 - Initiated program based on de-novo design leading small group of chemists
 - Program upgraded to lead optimization status in 6 months, research staff culminated to ~30 scientists o Identified 3 novel series of CCR2 antagonists
- Program chemist: NAE inhibitor program, oncology
 - Culminated in the discovery and selection of MLN4924 (NCT03772925), currently in multiple advanced oncology clinical trials
- Program chemist: receptor antagonist program, asthma

- Culminated in the discovery and selection of MLN6095, IND-enabled, licensed to Sanofi-Aventis
- Program chemist: polo-like kinase program, oncology
 - Culminated in discovery and selection of MLN0905, selected for clinical development

Education

Harvard University, Cambridge MA **2001-2003**

Post-Doctoral Fellow, NIH NRSA Fellowship; Advisor: Elias J. Corey, Nobel Laureate, Professor of Chemistry

University of Kansas, Lawrence KS **1996-2001**

Doctor of Philosophy, Chemistry; Advisor: Paul R. Hanson, Professor of Chemistry
University Most Outstanding Doctoral Dissertation

Wake Forest University, Winston-Salem NC **1992-1995**

Bachelor of Science, *Cum Laude*, Biology

Patents and Patent Applications

1. **Sprott, Kevin T.**; Moustakim, Moses; Saulnier, Mark G.; Steel, Richard J.; and Kass, Jorden. Stablix, Inc. **WO2023/122298**. Protein stabilizing compounds containing USP28 and/or USP25 targeting ligands.
2. Deshpande, Milind; Chen, Jesse J.; Saulnier, Mark G.; Karra, Srinivasa; Wiles, Jason A.; **Sprott, Kevin T.**; and Ray, Soumya. Avilar Therapeutics, Inc. **WO2023/009554**. Methods to reduce adverse effects of Gene or Biologics therapy.
3. **Sprott, Kevin T.**; Saulnier, Mark G.; Moustakim, Moses; Bowman, Brian; Kass, Jorden; and Steel, Richard J. Stablix, Inc. **WO2022/272133**. Protein stabilizing compounds containing USP7 ligands.
4. Wiles, Jason A.; Karra, Srinivasa; Saulnier, Mark G.; Chen, Jesse J.; **Sprott, Kevin T.**; and Ray, Soumya. Avilar Therapeutics, Inc. **WO2022/235699**. Potent ASGPR-binding compounds for the degradation of immunoglobulins and other proteins.
5. Deshpande, Milind; Saulnier, Mark G.; **Sprott, Kevin T.**; Chen, Jesse J.; Ray, Soumya; and Wiles, Jason A. Avilar Therapeutics, Inc. **WO2022/035997**. *In vivo* assembly of ASGPR binding therapeutics.
6. Saulnier, Mark G.; Chen, Jesse J.; Karra, Srinivasa; **Sprott, Kevin T.**; Wiles, Jason A.; and Ray, Soumya. Avilar Therapeutics, Inc. **WO2021/155317**. ASGPR-binding compounds for the degradation of extracellular proteins.
7. Marineau, Jason J.; **Sprott, Kevin**; Ciblat, Stephane; Roberts, Christopher; Zhang, Yi; Beaumier, Francis; Lepissier, Luce; Sow, Boubacar; Rahl, Peter B.; Larouche-Gauthier, Robin; and Brestler, Lauren. Syros Pharmaceuticals, Inc. **US2019/0048019**. Compounds for the modulation of MYC activity.

8. Marineau, Jason J.; Zahler, Robert; Ciblat, Stephane; Winter, Dana K.; Kabro, Anzhelika; Roy, Stephanie; Schmidt, Darby; Chuaqui, Claudio; Malojcic, Goran; Piras, Henri; Whitmore, Kenneth M.; Lund, Kate-Lyn; Sinko, Bill; and **Sprott, Kevin**. Syros Pharmaceuticals, Inc. **WO2018/013867**. Inhibitors of Cyclin-Dependent Kinase 7 (CDK7).
9. Roberts, Christopher; Zhang, Yi; Beaumier, Francis; Lepissier, Luce; Marineau, Jason J.; Rahl, Peter B.; **Sprott, Kevin**; Ciblat, Stephane; Sow, Boubacar; Larouche-Gauthier, Robin; and Berstler, Lauren. Syros Pharmaceuticals, Inc. **WO2016/197078**. Compounds for the modulation of MYC activity.
10. Roberts, Christopher; Zhang, Yi; Beaumier, Francis; Lepissier, Luce; Marineau, Jason J.; Rahl, Peter B.; **Sprott, Kevin**; Ciblat, Stephen; Sow, Boubacar; Larouche-Gauthier, Robin; and Berstler, Lauren. Syros Pharmaceuticals, Inc. **WO2016/196910**. Compounds for the modulation of MYC activity.
11. Ciblat, Stephane; Kabro, Anzhelika; Leblanc, Melissa; Leger, Serge; Marineau, Jason J.; Miller, Tom; Roy, Stephanie; Schmidt, Darby; Siddiqui, M. Arshad; **Sprott, Kevin**; Winter, Dana K.; Ripka, Amy; Li, Dansu; and Zhang, G. Syros Pharmaceuticals, Inc. **WO2016/058544**. Inhibitors of Cyclin-Dependent Kinase 7 (CDK7).
12. **Sprott, Kevin**; Marineau, Jason J.; Schmidt, Darby; Siddiqui, M. Arshad; Ciblat, Stephane; Roy, Stephanie; and Winter, Dana K. Syros Pharmaceuticals, Inc. **WO2015/154038**. Inhibitors of Cyclin-Dependent Kinase 7 (CDK7).
13. Marineau, Jason J.; **Sprott, Kevin**; and Schmidt, Darby. Syros Pharmaceuticals, Inc. **WO2015/154022**. Inhibitors of Cyclin-Dependent Kinase 7 (CDK7).

14. **Sprott, Kevin**; Marineau, Jason J.; Schmidt, Darby; Bradley, Michael; Ciblat, Stephane; Siddiqui, M. Arshad; Kabro, Anzhelika; Leblanc, Melissa; Leger, Serge; Roy, Stephanie; Winter, Dana K.; Miller, Tom; Ripka, Amy; and Li, Dansu. Syros Pharmaceuticals, Inc. **WO2015/154039**. Inhibitors of Cyclin-Dependent Kinase 7 (CDK7).
15. Ciblat, Stephane; Deroy, Patrick; Gray, Nathanael; Leblanc, Melissa; Marineau, Jason J.; Moore, Joel; **Sprott, Kevin**; Zhang, Tinghu; Siddiqui, M. Arshad; Kabro, Anzhelika; Leger, Serge; Miller, Tom; Roy, Stephanie; Schmidt, Darby; Winter, Dana K.; and Bradley, Michael. Syros Pharmaceuticals, Inc. **WO2015/058126**. Heteroaromatic compounds useful for the treatment for the treatment of proliferative diseases.
16. Ciblat, Stephane; Deroy, Patrick; Leblanc, Melissa; Marineau, Jason J.; Moore, Joel; Roy, Stephanie; Siddiqui, M. Arshad; **Sprott, Kevin**; Winter, Dana K.; Kabro, Anzheliika; Leger, Serge; Miller, Tom; Schmidt, Darby; and Bradley, Michael. Syros Pharmaceuticals, Inc. **WO2015/058163**. Heteroaromatic compounds useful for the treatment for the treatment of proliferative diseases.
17. **Sprott, Kevin**; Lewis, Michael; Choi, Hyeongwook; Fang, Frank; Shan, Mingde; Lazarova, Tsvetelina I.; Li, Lin; Siddiqui, Arshad M.; Larouche-Gathier, Robin; and Lemire, Alexandre. **US2014/0371285**. Therapeutic compounds and related methods of use.
18. Barden, Timothy; Hudson, Colleen; Jia, James; Kim, Charles; Graul, Regina; Mermerian, Ara; Moore, Joel; **Sprott, Kevin**; and Chien, Yueh-tyng. **US2013/0259830**. CRTH2 modulators.
19. **Sprott, Kevin**; Lewis, Michael; Choi, Hyeongwook; Fang, Frank; Shan, Mingde; Lazarova, Tsvetelina I.; Li, Lin; Siddiqui, M. Arshad; Larouche-

- Gauthier, Robin; and Lemire, Alexandre. **WO2013/103993**. Therapeutic compounds and related methods of use.
20. Hudson, Colleen; Barden, Timothy C.; Jia, James; Mermerian, Ara; Peng, Bo; Yang, Jane; Yu, Xiang Y.; **Sprott, Kevin**; and Fretzen, Angelika. Ironwood Pharmaceuticals, Inc. **WO2012/088469**. FAAH inhibitors.
21. Hudson, Colleen; Barden, Timothy C.; Jia, James; Mermerian, Ara; Peng, Bo; Yang, Jane; Yu, Xiang Y.; and **Sprott, Kevin**. Ironwood Pharmaceuticals, Inc. **WO2012/088431**. FAAH inhibitors.
22. Barden, Timothy; Hudson, Colleen; Jia, James; Kim, Charles; Graul, Regina; Mermerian, Ara; Moore, Joel; **Sprott, Kevin**; and Chien, Yueh-Tyng. Ironwood Pharmaceuticals, Inc. **WO2012/009134**. CRTH2 modulators.
23. **Sprott, Kevin**; Talley, John Jeffrey; Yang, Jane; Peng, Bo. Ironwood Pharmaceuticals, Inc. **WO2011/071996**. FAAH inhibitors.
24. Rohde, Jason; Peng, Bo; Nakai, Takashi; **Sprott, Kevin**; Mermerian, Ara; Schairer, Wayne C; and Galen, John C. Ironwood Pharmaceuticals, Inc. **WO2011/100359**. Cannabinoid agonists.
25. Mermerian, Ara; Peng, Bo; Hudson, Colleen; Kim, Charles; Moore, Joel; Rohde, Jason; **Sprott, Kevin**; Graul, Regina; Nakai, Takashi; Jia, James; and Bartolini, Wilmin. Ironwood Pharmaceuticals, Inc. **WO2011/079007**. CRTH2 modulators.
26. **Sprott, Kevin**; Rohde, Jason; Nakai, Takashi; Peng, Bo; Talley, and John Jeffrey. Ironwood Pharmaceuticals, Inc. **WO2011/006066**. CB receptor agonists.
27. **Sprott, Kevin**; Talley, John Jeffrey; Pearson, James Philip; Milne, and Todd G. Ironwood Pharmaceuticals, Inc. **WO2008/157740**. FAAH inhibitors.
28. Talley, John Jeffrey; **Sprott, Kevin**; Pearson, James Philip; Milne, G. Todd; Schairer, Wayne; Yang, Jing Jing; Kim, Charles; Barden, Timothy;

- Lundigran, Regina; Mermerian, Ara; and Currie, Mark G. Ironwood Pharmaceuticals, Inc. **WO2008/019357**. Indole compounds.
29. Bartolini, Wilmin; Cali, Brian M.; Chen, Barbara; Chien, Yueh-Tyng; Currie, Mark G.; Milne, G. Todd; Pearson, James Philip; Talley, John Jeffrey; Yang, Jing Jing; Zimmerman, Craig; Kim, Charles; **Sprott, Kevin**; Barden, Timothy; Lundigran, Regina; and Mermerian, Ara. Ironwood Pharmaceuticals, Inc. **WO2007/070892**. Useful indole compounds.
30. **Sprott, Kevin**; Raman, Prakash; Ghosh, Shomir; Elder, Amy M.; Griffiths, Sian; Soucy, Francois; and Ye, Qing. Millennium Pharmaceuticals, Inc. **WO2007/053495**. Compounds useful as antagonists of CCR2.
31. Elder, Amy M.; Ghosh, Shomir; Griffiths, Sian; Raman, Prakash; Soucy, Francois; **Sprott, Kevin**; and Ye, Qing. Millennium Pharmaceuticals, Inc. **WO2007/053499**. Compounds useful as antagonists of CCR2.
32. Ghosh, Shomir; Raman, Prakash; **Sprott, Kevin**; Elder, Amy M.; Griffiths, Sian; Soucy, Francois; and Ye, Qing. Millennium Pharmaceuticals, Inc. **WO2007/053498**. Compounds useful as antagonists of CCR2.
33. Ghosh, Shomir; Elder, Amy M.; Carson, Kenneth G.; **Sprott, Kevin T.**; Harrison, Sean J.; Hicks, Frederick A.; Renou, Christelle C.; and Reynolds, Dominic. Millennium Pharmaceuticals, Inc. **WO2005/100321**. PGD2 receptor antagonists for the treatment of inflammatory diseases.
34. Ghosh, Shomir; Elder, Amy M.; Carson, Kenneth G.; **Sprott, Kevin**; and Harrison, Sean. Millennium Pharmaceuticals, Inc. **WO2004/032848**. PGD2 receptor antagonists for the treatment of inflammatory diseases.
35. Hanson, Paul R.; **Sprott, Kevin T.**; McReynolds, Matthew D. The University of Kansas. **WO2002/014344**. Amino acid-derived cyclic phosphonamides and methods of synthesizing the same.

36. **Sprott, Kevin T.**; Hanson, Paul R. The University of Kansas. **WO2002/014331**. Amino acid-derived cyclic phosphonamides and methods of synthesizing the same.

Peer-reviewed Publications

1. Hu S, Marineau JJ, Rajagopal N, Hamman KB, Choi YJ, Schmidt DR, Ke N, Johannessen L, Bradley MJ, Orlando DA, Alnemy SR, Ren Y, Ciblat S, Winter DK, Kabro A, **Sprott KT**, Hodgson JG, Fritz CC, Carulli JP, di Tomaso E, and Olson ER. Discovery and Characterization of SY-1365, a Selective, Covalent Inhibitor of CDK7. *Cancer Research*. **2019** Jul 1, 79(13):3479-3491.
2. Duffey MO, Vos TJ, Adams R, Alley J, Anthony J, Barrett C, Bharathan I, Bowman D, Bump NJ, Chau R, Cullis C, Driscoll DL, Elder A, Forsyth N, Frazer J, Guo J, Guo L, Hyer ML, Janowick D, Kulkarni B, Lai SJ, Lasky K, Li G, Li J, Liao D, Little J, Peng B, Qian MG, Reynolds DJ, Rezaei M, Scott MP, Sells TB, Shinde V, Shi QJ, Sintchak MD, Soucy F, **Sprott KT**, Stroud SG, Nestor M, Visiers I, Weatherhead G, Ye Y, and D'Amore N. Discovery of a potent and orally bioavailable benzolactam-derived inhibitor of Polo-like kinase 1 (MLN0905). *Journal of Medicinal Chemistry*. **2012** Jan 12, 55(1):197-208.
3. **Sprott KT**, and Corey EJ. A new cationic, chiral catalyst for highly enantioselective Diels-Alder reactions. *Organic Letters*. **2003** Jul 10, 5(14):2465-7.
4. McReynolds MD, **Sprott KT**, and Hanson PR. A concise route to structurally diverse DMP 323 analogues via highly functionalized 1,4-diamines. *Organic Letters*. **2002** Dec 26, 4(26):4673-6.

5. Moore JD, **Sprott KT**, and Hanson PR. Conformationally constrained alpha-boc-aminophosphonates via transition metal-catalyzed/curtius rearrangement strategies. *Journal of Organic Chemistry*. **2002** Nov 15, 67(23):8123-9.
6. Wanner J, **Sprott KT**, Poon K, Harned A, Probst D, Sheriff B, Petz M, and Hanson PR. Ring-opening metathesis polymerization approach to phosphorous-containing biololigomers. *Phosphorus, Sulfur, and Silicon, and the Related Elements*. **2002**, 177(8-9):1971-72.
7. **Sprott KT**, McReynolds MD, and Hanson PR. Ring-closing metathesis strategies to P-heterocycles. *Phosphorus, Sulfur, and Silicon, and the Related Elements*. **2002**, 177(6-7):1807-09.
8. Moore JD, **Sprott KT**, Wroblewski AD, and Hanson PR. Double diastereoselective intramolecular cyclopropanation to P-chiral [3.1.0]-bicyclic phosphonates. *Organic Letters*. **2002** Jul 11, 4(14):2357-60.
9. **Sprott KT**, McReynolds MD, and Hanson PR. A temporary phosphorus tether/ring-closing metathesis strategy to functionalized 1,4-diamines. *Organic Letters*. **2001** Nov 29, 3(24):3939-42.
10. Moore JD, **Sprott KT**, and Hanson PR. New Strategies to Cyclic alpha-thiophosphonates. *Synthetic Letters*. **2001**, 2001(5):0605-0608.
11. **Sprott KT**, McReynolds MD, and Hanson PR. Ring-Closing Metathesis Strategies to Amino Acid-Derived P-Heterocycles. *Synthesis*. **2001**, 2001(4):0612-0620.
12. **Sprott KT**, and Hanson PR. The synthesis of sterically demanding amino acid-derived cyclic phosphonamides. *Journal of Organic Chemistry*. **2000** Nov 17;65(23):7913-8.
13. Hanson P, Wanner J, Probst DA, Harned A, Poon KW, Robinson RE, and **Sprott KT**. Metathesis strategies to functionalized biopolymers. *Polymeric Materials Science and Engineering*. **2001**, 84:863.

14. **Sprott KT**. Synthetic methods to new organophosphorus compounds: transition metal-catalyzed approaches. ProQuest. **2001**, 62(4):343 pages.
15. **Sprott KT**, and Hanson PR. The Synthesis of Sterically Demanding Amino Acid-Derived Cyclic Phosphonamides. Journal of Organic Chemistry. **2000**, 65(23):7913-18.
16. **Sprott KT**, and Hanson PR. The Synthesis of P-Chiral Amino Acid-Derived Phosphonamidic Anhydrides. Journal of Organic Chemistry. **2000**, 65(15):4721-28.
17. Hanson PR, **Sprott KT**; and Wroblewski AD. Intramolecular cyclopropanation reactions en route to novel P-heterocycles. Tetrahedron Letters. **1999**, 40(8):1455-58.

Conference Abstracts and Presentations

1. Hanson PR, Moore JD, **Sprott KT**. Double diastereotopic differentiation on a phosphonate template. Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, **2001** August 26-30, ORGN-573.
2. Hanson PR, **Sprott, KT**, and McReynolds MD. Phosphorus-based temporary tether-RCM approach to heterocyclic enzyme inhibitors. Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, **2001** August 26-30, ORGN-572.
3. Hanson P, Wanner J, Probst DA, Harned A, Poon KW, Robinson RE, and **Sprott KT**. Metathesis strategies to functionalized biopolymers. Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, **2001** April 1-5, PMSE-478.

4. Moore JD, **Sprott KT**, and Hanson PR. Rhodium (II)-catalyzed strategies to diverse phosphonates. Abstracts of Papers, 220th ACS National Meeting, Washington, DC, United States, **2000** August 20-24, ORGN-466.
5. McReynolds MD, **Sprott KT**, and Hanson PR. Metathesis approaches to 7-membered P-heterocycles. Abstracts of Papers, 220th ACS National Meeting, Washington, DC, United States, **2000** August 20-24, ORGN-206.
6. **Sprott KT**, Hanson PR, McReynolds MD, and Moore JD. Metathesis strategies toward heterocyclic phosphorus compounds. Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, **2000** March 26-30, ORGN-825.
7. Hanson PR, Stoianova D, **Sprott KT**, Dougherty JM, McReynolds MD, and Moore JD. Metathesis strategies on phosphorus templates. Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, **2000** March 26-30, ORGN-017.
8. Hanson PR, Dougherty JM, **Sprott, KT**, and Stoianova DS. Ring-closing metathesis strategy to structurally diverse phosphorus compounds. Book of Abstracts, 218th ACS National Meeting, New Orleans, **1999** Aug. 22-26, ORGN-305.
9. Hanson PR, and **Sprott KT**. Synthesis of amino acid-derived phosphonamidic anhydrides. Book of Abstracts, 218th ACS National Meeting, New Orleans, **1999** Aug. 22-26, ORGN-221.
10. Dougherty JM, Hanson PR, Probst, DA, Robinson RE, **Sprott KT**, and Stoianova DS. Transition metal catalyzed approaches to complex phosphorus and sulfonamide compounds. Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., **1999** March 21-25, ORGN-014.
11. Hanson PR, Dougherty JM, Probst DA, Robinson RE, **Sprott K**, and Stoianova DS. Transition-metal-catalyzed approaches to structurally diverse

phosphorus- and sulfur-containing motifs. Book of Abstracts, 218th ACS National Meeting, New Orleans, **1999** Aug. 22-26, ORGN-036.

12.Hanson PR, **Sprott, KT**, and Stoianova DS. Organometallic approaches to complex phosphorus compounds. Book of Abstracts, 216th ACS National Meeting, Boston, **1998** August 23-27, ORGN-513.

13.Hanson PR, and **Sprott KT**. Intramolecular cyclopropanation reactions on a phosphonate template. Book of Abstracts, 216th ACS National Meeting, Boston, **1998** August 23-27, ORGN-124.