

PYRIDAZINONE COMPOUNDS AND USES THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of US Provisional Application Serial Number 62/756,553 filed November 6, 2018, which is hereby incorporated herein by reference in its entirety.

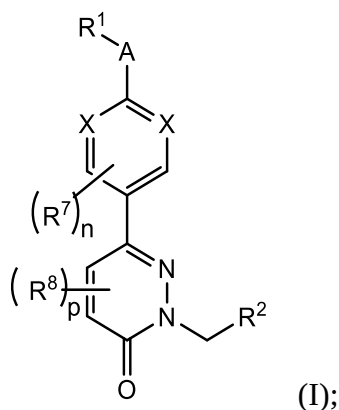
BACKGROUND OF THE INVENTION

[0002] Skeletal muscle is the largest organ system in the human body, serving two primary purposes. The first is force production to enable muscle contraction, locomotion, and postural maintenance; the second is glucose, fatty acid and amino acid metabolism. The contraction of skeletal muscle during every-day activity and exercise is naturally connected to muscle stress, breakdown and remodeling which is important for muscle adaptation. In individuals with neuromuscular conditions, such as Duchenne Muscular Dystrophy (DMD), muscle contractions lead to continued rounds of amplified muscle breakdown that the body struggles to repair. Eventually, as patients age, a pathophysiological process emerges that leads to excess inflammation, fibrosis, and fatty deposit accumulation in the muscle, portending a steep decline in physical function and contribution to mortality.

[0003] DMD is a genetic disorder affecting skeletal muscle and is characterized by progressive muscle degeneration and weakness. There remains a need for treatments that reduce muscle breakdown in patients with neuromuscular conditions such as DMD.

SUMMARY

[0003a] In an aspect of the present disclosure, there is provided a compound represented by Formula (I):



or a salt thereof, wherein:

each X is independently selected from C(R³), N, and N⁺(-O⁻) wherein at least one X is N or N⁺(-O⁻);
A is selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O=S, =N(R¹⁰), -CN, C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, wherein C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl are each optionally substituted with one or more R⁹; or

R¹ together with R³ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁵ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁴ form a 3- to 10- membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R⁹;

R² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and when R² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O⁻;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more R⁹;

R³, R⁵, and R⁶ are each independently selected from:

hydrogen, halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or

R³ together with R¹ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R⁵ together with R¹ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹;

R⁴ is independently selected from:

hydrogen; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or R⁴ together with R¹ form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

R⁷ and R⁸ are independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, and C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from:

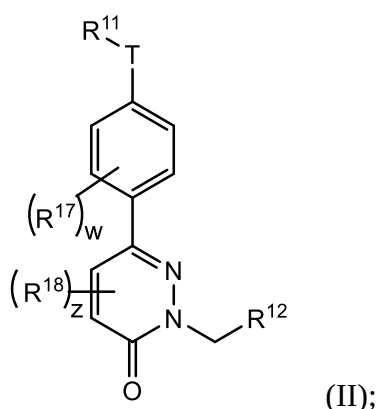
hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -

NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and C₁₋₆ haloalkyl;

[0003b] In another aspect of the present disclosure, there is provided a compound represented by Formula (II):



or a salt thereof, wherein,

T is selected from -O-, -NR¹⁴-, -CR¹⁵R¹⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂;

R¹¹ is selected from:

C₁₋₅ haloalkyl optionally further substituted with one or more substituents independently selected from -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, =O, =S, -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R¹⁹;

R¹² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN; and when R¹² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O-;

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂,

-N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R¹⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more -R¹⁹;

R¹⁴ is selected from:

hydrogen, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁵ and R¹⁶ is independently selected from:

hydrogen, halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁷ and R¹⁸ is independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁹ is independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), and -CN;

each R²⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -

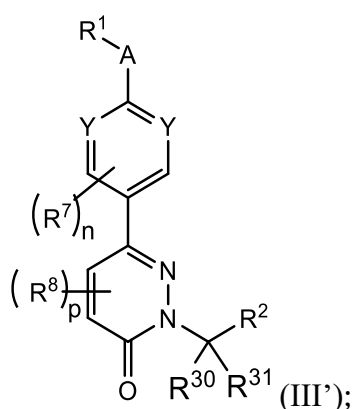
OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

w is 0, 1, or 2; and

z is 0, 1, or 2.

[0003c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound or salt disclosed herein and a pharmaceutically acceptable excipient.

[0003d] In another aspect of the present disclosure, there is provided a use of a compound or salt of Formula (III'):



or a salt thereof, in the manufacture of a medicament for treating activity-induced muscle damage, a neuromuscular condition, or a movement disorder, wherein:

each Y is independently selected from C(R³), N, and N⁺(-O⁻);

A is absent or selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -

OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; or

R¹ together with R³ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁵ form a 3- to 10- membered heterocycle or saturated C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or saturated C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁴ form a 3- to 10- membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R⁹; and

when A is -NR⁴-, R¹ is additionally selected from hydrogen, and when A is -C(O)-, R¹ is additionally selected from -N(R¹⁰)₂ and -OR¹⁰;

when A is absent R¹ is further selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, and -CN;

R² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and when R² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O-;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more R⁹;

each R³, R⁵, and R⁶ is independently selected from:

hydrogen, halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or

R³ together with R¹ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; R⁵ together with R¹ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹;

R⁴ is independently selected from:

hydrogen; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or R⁴ together with R¹ form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

each R⁷ and R⁸ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl),

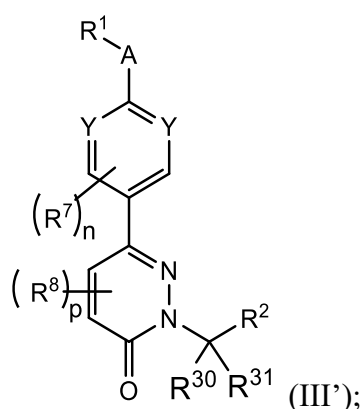
C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

R³⁰ and R³¹ are independently selected from R¹⁰ or R³⁰ and R³¹ come together to form a C₃₋₇ carbocycle, wherein the 3- to 7- membered heterocycle, wherein C₃₋₇ carbocycle and 3- to 7- membered heterocycle are optionally substituted with R⁹;

n is 0, 1, or 2; and

p is 0, 1, or 2.

[0003e] In a further aspect of the present disclosure, there is provided a compound or salt of Formula (III'):



or a salt thereof, for use in treating activity-induced muscle damage, a neuromuscular condition, or a movement disorder, wherein:

each Y is independently selected from C(R³), N, and N⁺(-O⁻);

A is absent or selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -

OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; or

R¹ together with R³ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁵ form a 3- to 10- membered heterocycle or saturated C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or saturated C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁴ form a 3- to 10- membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R⁹; and

when A is -NR⁴-, R¹ is additionally selected from hydrogen, and when A is -C(O)-, R¹ is additionally selected from -N(R¹⁰)₂ and -OR¹⁰;

when A is absent R¹ is further selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, and -CN;

R² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and when R² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O-;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more R⁹;

each R³, R⁵, and R⁶ is independently selected from:

hydrogen, halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or

R³ together with R¹ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; R⁵ together with R¹ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹;

R⁴ is independently selected from:

hydrogen; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or R⁴ together with R¹ form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

each R⁷ and R⁸ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl),

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

R³⁰ and R³¹ are independently selected from R¹⁰ or R³⁰ and R³¹ come together to form a C₃₋₇ carbocycle, wherein the 3- to 7- membered heterocycle, wherein C₃₋₇ carbocycle and 3- to 7-membered heterocycle are optionally substituted with R⁹;

n is 0, 1, or 2; and

p is 0, 1, or 2.

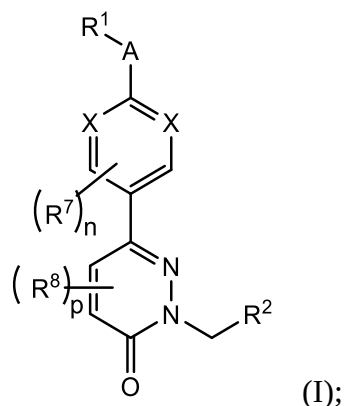
[0004] The present disclosure generally relates to substituted pyridazinone compounds or salts of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), or (IIa) and pharmaceutical compositions thereof. The substituted pyridazinone compounds or salts of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), or (IIa) disclosed herein may be used to treat or prevent neuromuscular diseases. In some examples, a compound or salt of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), or (IIa) is an inhibitor of skeletal muscle contraction. In some examples, a compound or salt of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), or (IIa) is an inhibitor of myosin. In some examples, a compound or salt of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), or (IIa) is an inhibitor of skeletal muscle myosin II.

[0005] In some examples, methods of treating a movement disorder may comprise administering a compound or salt of any one of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), (IIa), (III), or (III') to inhibit skeletal muscle myosin II. In some examples, said movement disorder comprises muscle spasticity. In some examples, said muscle spasticity may be selected from spasticity associated

with multiple sclerosis, Parkinson's disease, Alzheimer's disease, or cerebral palsy, or injury, or a traumatic event such as stroke, traumatic brain injury, spinal cord injury, hypoxia, meningitis, encephalitis, phenylketonuria, or amyotrophic lateral sclerosis.

[0006] The present disclosure provides compound and salts thereof for use in treating disease. In certain examples, the present disclosure provides a compound or salt of Formula (I), (Ia), (Ib), (Ic), (Id), (II) or (IIa), pharmaceutical compositions thereof as well as methods of use in the treatment of disease.

[0007] In certain examples, the present disclosure provides a compound represented by Formula (I):



or a salt thereof, wherein:

each X is independently selected from C(R³), N, and N⁺(-O⁻) wherein at least one X is N or N⁺(-O⁻);

A is selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O=S, =N(R¹⁰), -CN, C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, wherein C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl are each optionally substituted with one or more R⁹; or

R¹ together with R³ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted

form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

R⁷ and R⁸ are independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, and C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and C₁₋₆ haloalkyl;

n is 0, 1, or 2; and

p is 0, 1, or 2.

[0008] In certain examples, the present disclosure provides a compound represented by Formula (II):

hydrogen, halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁷ and R¹⁸ is independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁹ is independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), and -CN;

each R²⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

w is 0, 1, or 2; and

z is 0, 1, or 2.

[0009] In certain examples, the present disclosure provides a method of treating activity-induced muscle damage, comprising administering to a subject in need thereof a compound or salt of Formula (III'):

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

R³⁰ and R³¹ are independently selected from R¹⁰ or R³⁰ and R³¹ come together to form a C₃₋₇

carbocycle, wherein the 3- to 7- membered heterocycle, wherein C₃₋₇ carbocycle and 3- to 7-membered heterocycle are optionally substituted with R⁹;

n is 0, 1, or 2; and

p is 0, 1, or 2.

[0010] In certain examples, the present disclosure provides a method of treating a neuromuscular condition or treating activity-induced muscle damage or of inhibiting muscle myosin II, comprising administering to a subject in need thereof a compound or salt of any one of Formulas (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), and (IIa).

[0011] In certain examples, the present disclosure provides a method of treating a movement disorder, comprising administering to a subject in need thereof a compound or salt of any one of Formulas (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), and (IIa).

[0012] In certain examples, the present disclosure provides a pharmaceutical composition comprising a compound or salt of any one Formulas (I), (Ia), (Ib), (Ic), (Id), (Ie), (II), and (IIa) or a pharmaceutically acceptable excipient.

INCORPORATION BY REFERENCE

[0013] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings (also “Figure” and “FIG.” herein), of which:

[0015] FIG.1 depicts excessive contraction-induced injuries, which precede the inflammation and irreversible fibrosis that characterizes late-stage DMD pathology;

[0016] FIG.2 depicts N-benzyl-p-tolyl-sulfonamide (BTS), an inhibitor of fast-fiber skeletal muscle myosin, has been shown to protect muscles from pathological muscle derangement in embryos from zebrafish model of DMD;

[0017] FIG.3 depicts the force decrease pre injury at 100Hz for various compounds of the disclosure;

[0018] FIG.4 depicts the post injury force decrease at 175 Hz for various compounds of the disclosure;

[0019] FIG.5 depicts mid lengthening force drop for various compounds of the disclosure; and

[0020] FIG.6 depicts the TA mass increase after injury for various compounds of the disclosure.

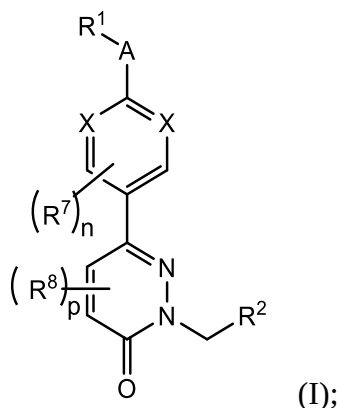
DETAILED DESCRIPTION OF THE INVENTION

[0021] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the

CLAIMS

WHAT IS CLAIMED IS:

1. A compound represented by Formula (I):



or a salt thereof, wherein:

each X is independently selected from C(R³), N, and N⁺(-O⁻) wherein at least one X is N or N⁺(-O⁻);

A is selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O=S, =N(R¹⁰), -CN, C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, wherein C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl are each optionally substituted with one or more R⁹; or

R¹ together with R³ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁵ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁴ form a 3- to 10-

membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R⁹;

R² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and when R² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O⁻;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more R⁹;

R³, R⁵, and R⁶ are each independently selected from:

hydrogen, halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or

R³ together with R¹ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R⁵ together with R¹ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹;

R⁴ is independently selected from:

hydrogen; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or R⁴ together with R¹ form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

R⁷ and R⁸ are independently selected from:

halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, $-CN$, and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and $-CN$;

each R^9 is independently selected from:

halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-C(O)R^{10}$, $-C(O)N(R^{10})_2$, $-N(R^{10})C(O)R^{10}$, $-N(R^{10})C(O)N(R^{10})_2$, $-OC(O)N(R^{10})_2$, $-N(R^{10})C(O)OR^{10}$, $-C(O)OR^{10}$, $-OC(O)R^{10}$, $-S(O)R^{10}$, $-S(O)_2R^{10}$, $-NO_2$, $=O$, $=S$, $=N(R^{10})$, and $-CN$; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-C(O)R^{10}$, $-C(O)N(R^{10})_2$, $-N(R^{10})C(O)R^{10}$, $-N(R^{10})C(O)N(R^{10})_2$, $-OC(O)N(R^{10})_2$, $-N(R^{10})C(O)OR^{10}$, $-C(O)OR^{10}$, $-OC(O)R^{10}$, $-S(O)R^{10}$, $-S(O)_2R^{10}$, $-NO_2$, $=O$, $=S$, $=N(R^{10})$, and $-CN$;

each R^{10} is independently selected from:

hydrogen; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-CN$, $-OH$, $-SH$, $-NO_2$, $-NH_2$, $=O$, $=S$, $-O-C_{1-6}$ alkyl, $-S-C_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl) $_2$, $-NH(C_{1-6}$ alkyl), C_{3-10} carbocycle, 3- to 10-membered heterocycle; and

C_{3-10} carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-CN$, $-OH$, $-SH$, $-NO_2$, $-NH_2$, $=O$, $=S$, $-O-C_{1-6}$ alkyl, $-S-C_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl) $_2$, $-NH(C_{1-6}$ alkyl), C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, and C_{1-6} haloalkyl;

n is 0, 1, or 2; and

p is 0, 1, or 2.

2. The compound or salt of claim 1, wherein A is selected from $-O-$, $-NR^4-$, and $-CR^5R^6-$.

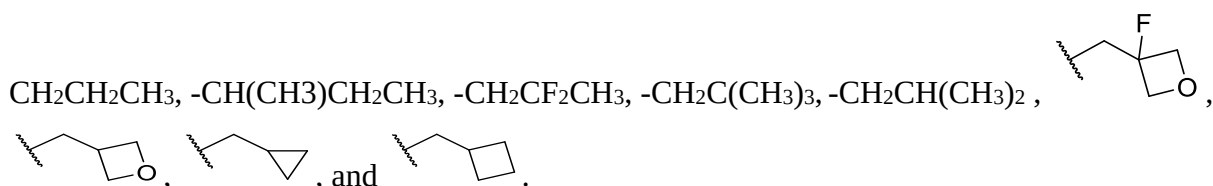
3. The compound or salt of claim 1, wherein R^1 is selected from:

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-C(O)R^{10}$, $-C(O)N(R^{10})_2$, $-N(R^{10})C(O)R^{10}$, $-CN$, C_{3-7} carbocycle and 3- to 7-membered heterocycle, wherein the C_{3-7} carbocycle and 3- to 7-membered heterocycle are each optionally substituted with one or more R^9 ; and

C₃₋₇ carbocycle optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -CN, C₁₋₆ alkyl, and C₁₋₆ haloalkyl; or

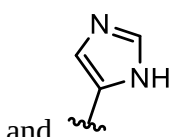
or R¹ together with R⁴ form a 3- to 6- membered heterocycle, wherein the 3- to 6- membered heterocycle is optionally substituted with one or more R⁹.

4. The compound or salt of claim 1, wherein R¹ is selected from C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹.
5. The compound or salt of claim 1, wherein R¹ is selected from C₁₋₃ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹.
6. The compound of salt of claim 1, wherein R¹ is selected from -CHF₂, -CH(CH₃)₂, -CH₂CH(CH₃)₂, -CH₂CF(CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂OCH₃, -CH₂CH₂OCF₃, -CH₂C(CH₃)₂OCH₃, -CH₂SCH₃, -CH₂CH₂SCH₃, -CH₂CH(CH₃)SCH₃, -CH₃, -CH₂CH₃, -

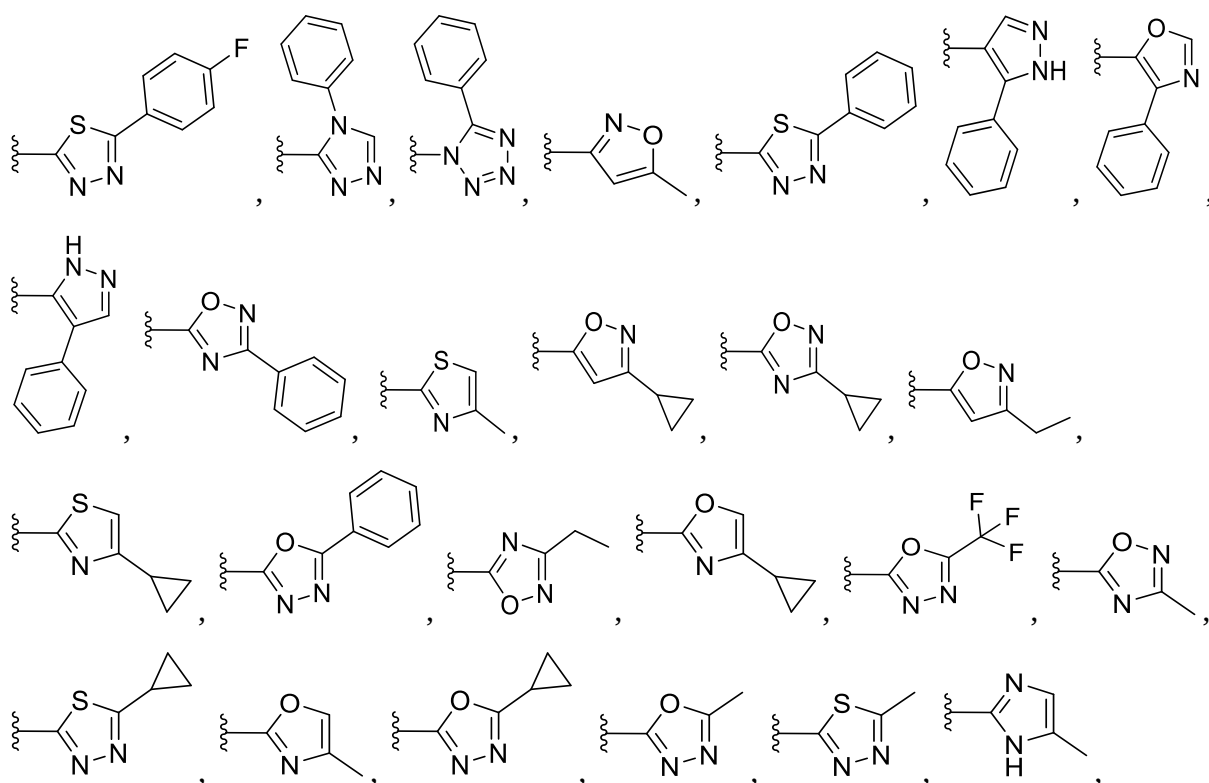


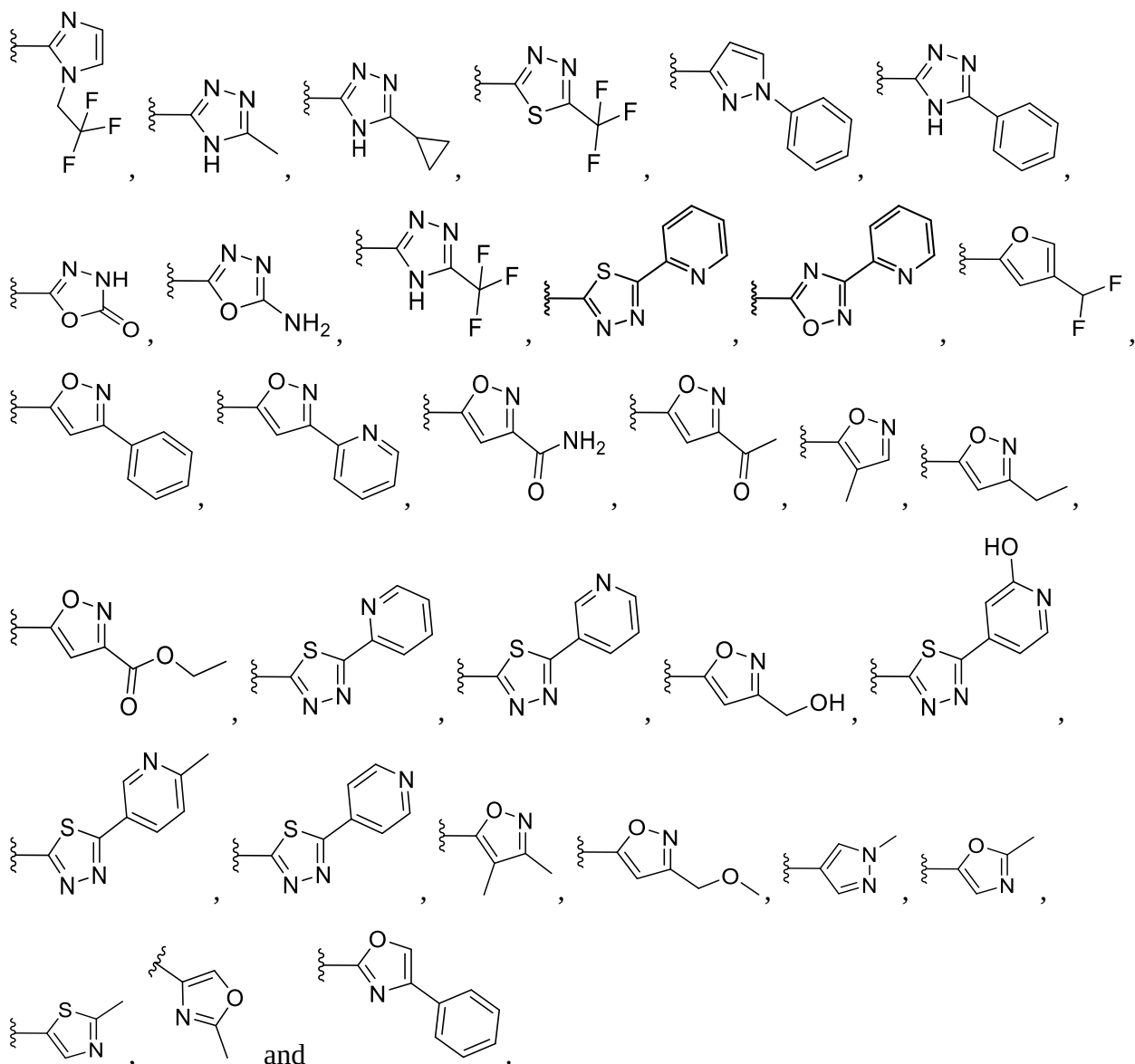
7. The compound or salt of claim 1, wherein R² is selected from optionally substituted 5- or 6-membered monocyclic heteroaryl and optionally substituted 9-membered bicyclic heteroaryl.
8. The compound or salt of claim 1, wherein R² is selected from isoxazole, oxazole, thiadiazole, triazole, isothiazole, tetrazole, pyrazole, pyrrole, furan, imidazole, oxadiazole, thiazole, pyridine, pyridazine, pyrimidine, pyrazine, tetrazine, benzoxazole, benzothiazole, benzimidazole, indole, indazole, and imidazopyridine, any of which is optionally substituted.
9. The compound or salt of claim 1, wherein R² is selected from optionally substituted 5-membered heteroaryl.

Chemical structures of furan, imidazole, and oxazole, each with a wavy line indicating a point of attachment.



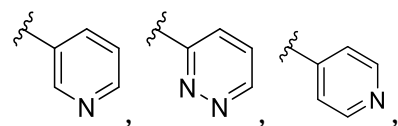
The image shows two chemical structures. The structure on the left is 2-phenylisobenzoxazole, which consists of a benzene ring fused to an isobenzoxazole ring. The structure on the right is 2-isobenzoxazolylphenyl, which consists of a benzene ring attached to an isobenzoxazole ring at the 2-position. Both structures have wavy lines indicating attachment points at the 4-position of the benzene ring and the 5-position of the isobenzoxazole ring.

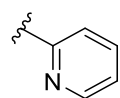
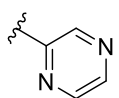




12. The compound or salt of claim 1, wherein R^2 is selected from optionally substituted 6-membered heteroaryl.
13. The compound or salt of claim 1, wherein R^2 is selected from optionally substituted pyridine, optionally substituted pyrimidine, optionally substituted pyridine N-oxide, optionally substituted pyridazine, and optionally substituted pyrimidine N-oxide.

14. The compound or salt of claim 1, wherein R^2 is selected from

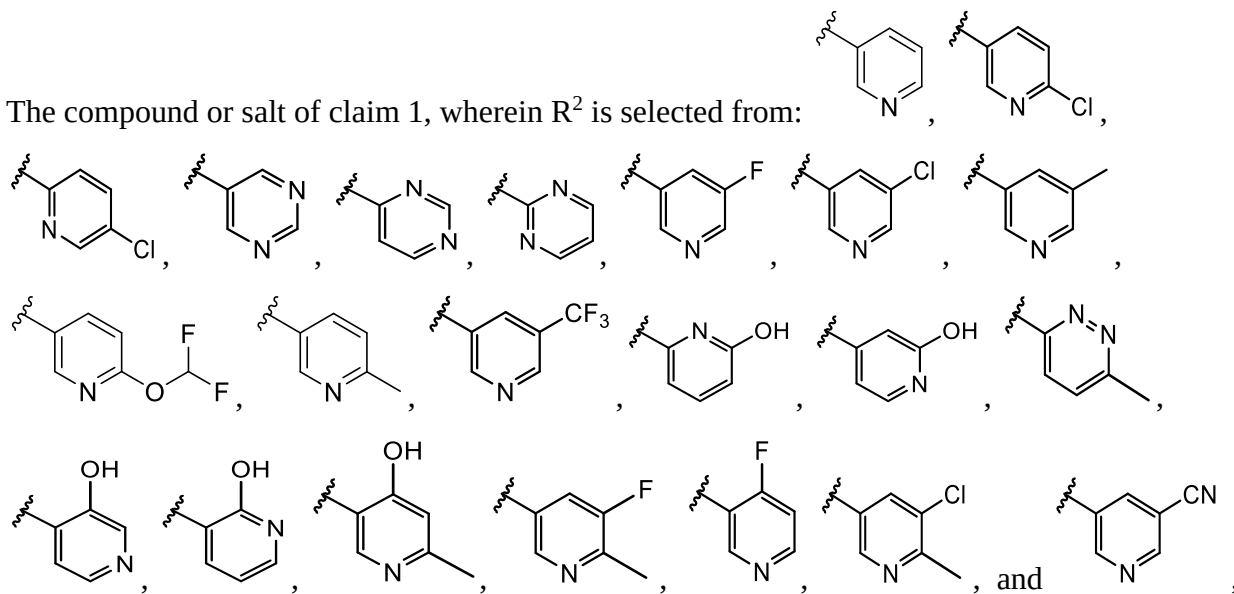


- , and , and  any of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -CN, and a substituent on a nitrogen atom of the pyridyl is optionally selected from -O⁻; and

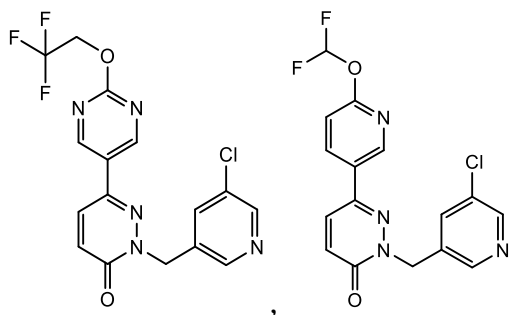
C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen and -OR¹⁰.

15. The compound or salt of claim 1, wherein R² is selected from:

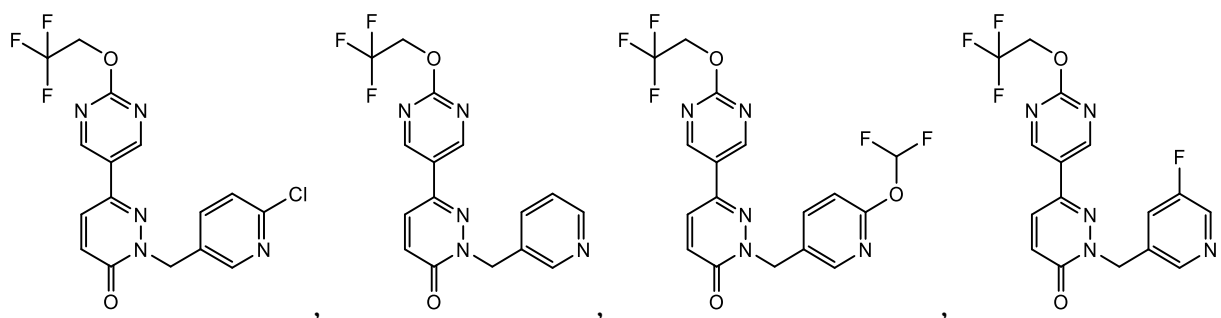


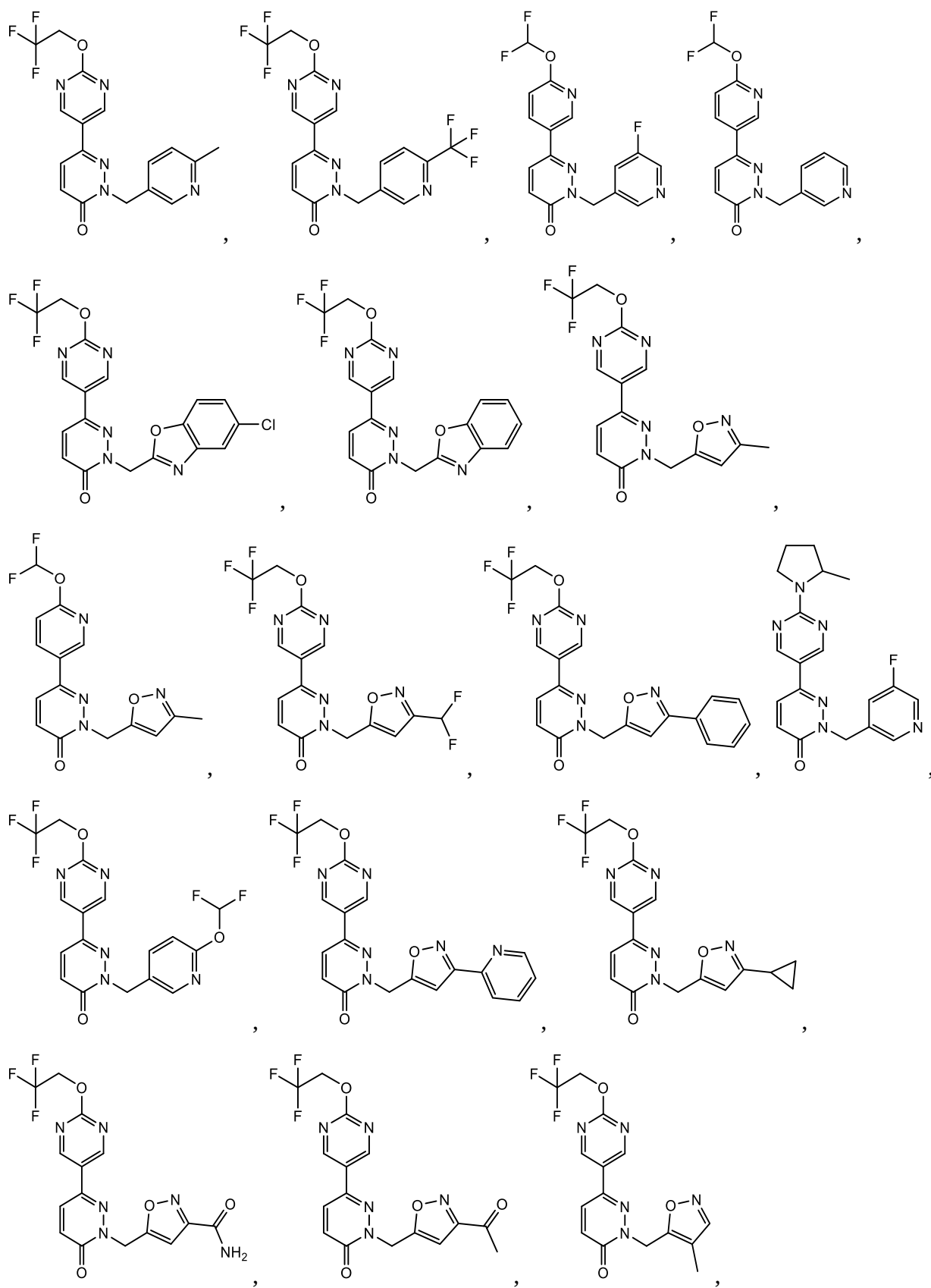
any one of which is optionally substituted.

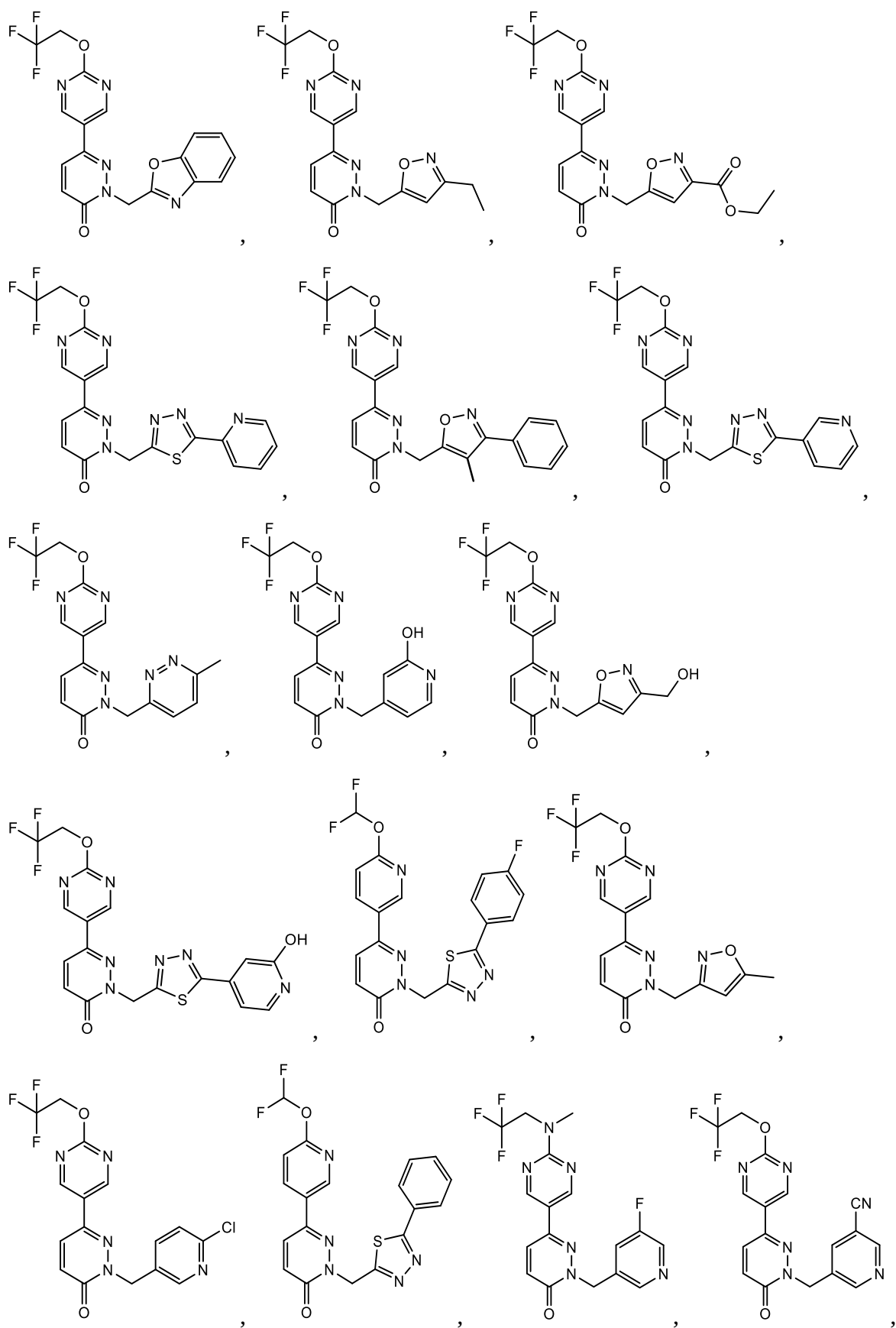
16. The compound or salt of claim 1, wherein n is 0 and p is 0.

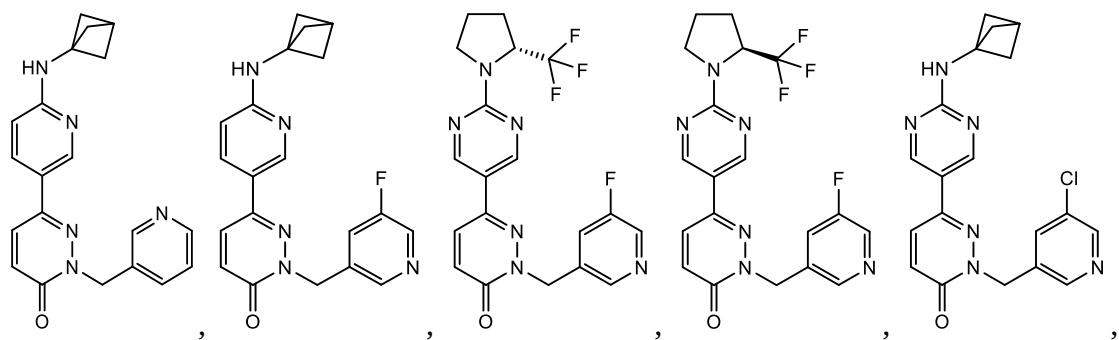
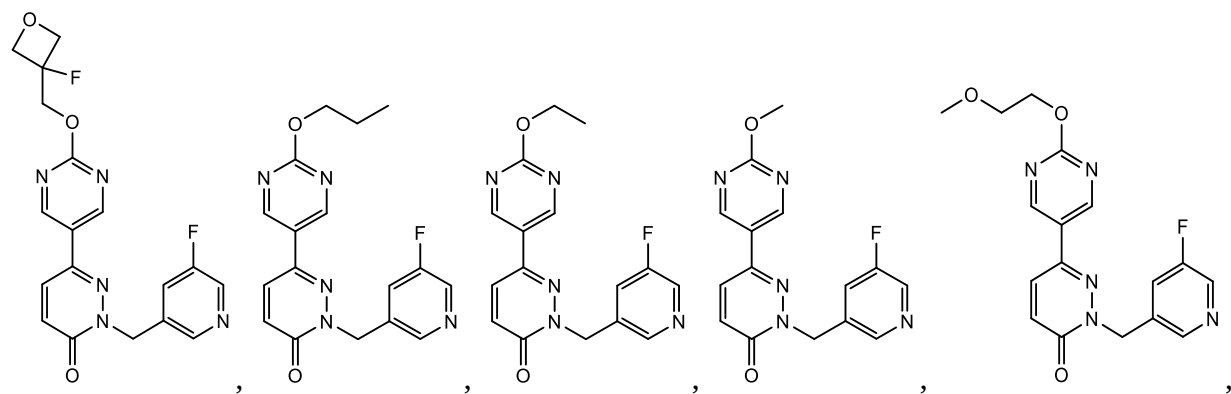
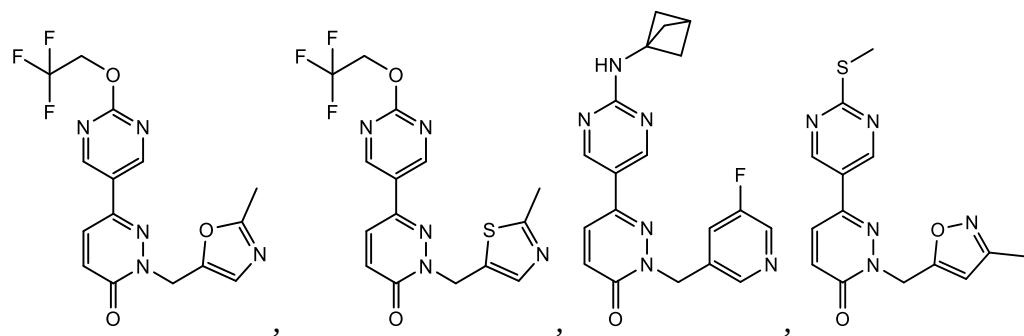
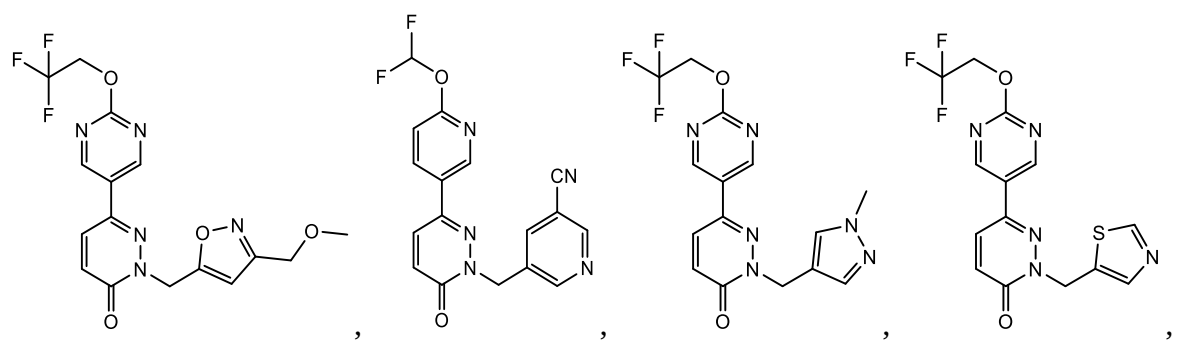
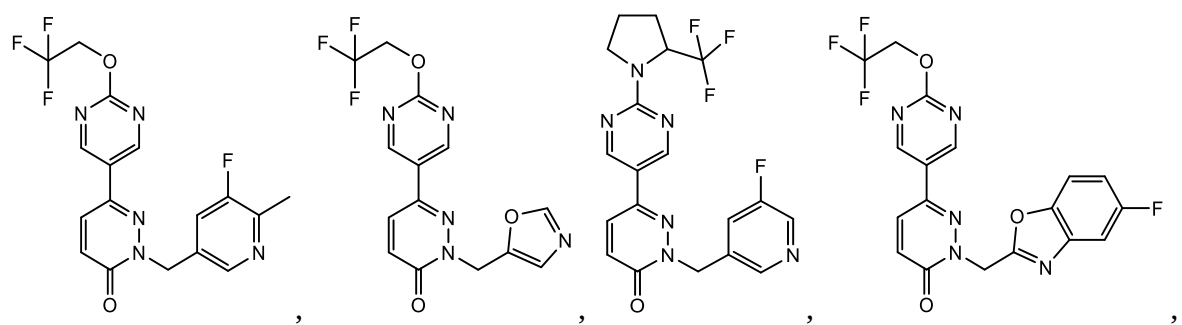


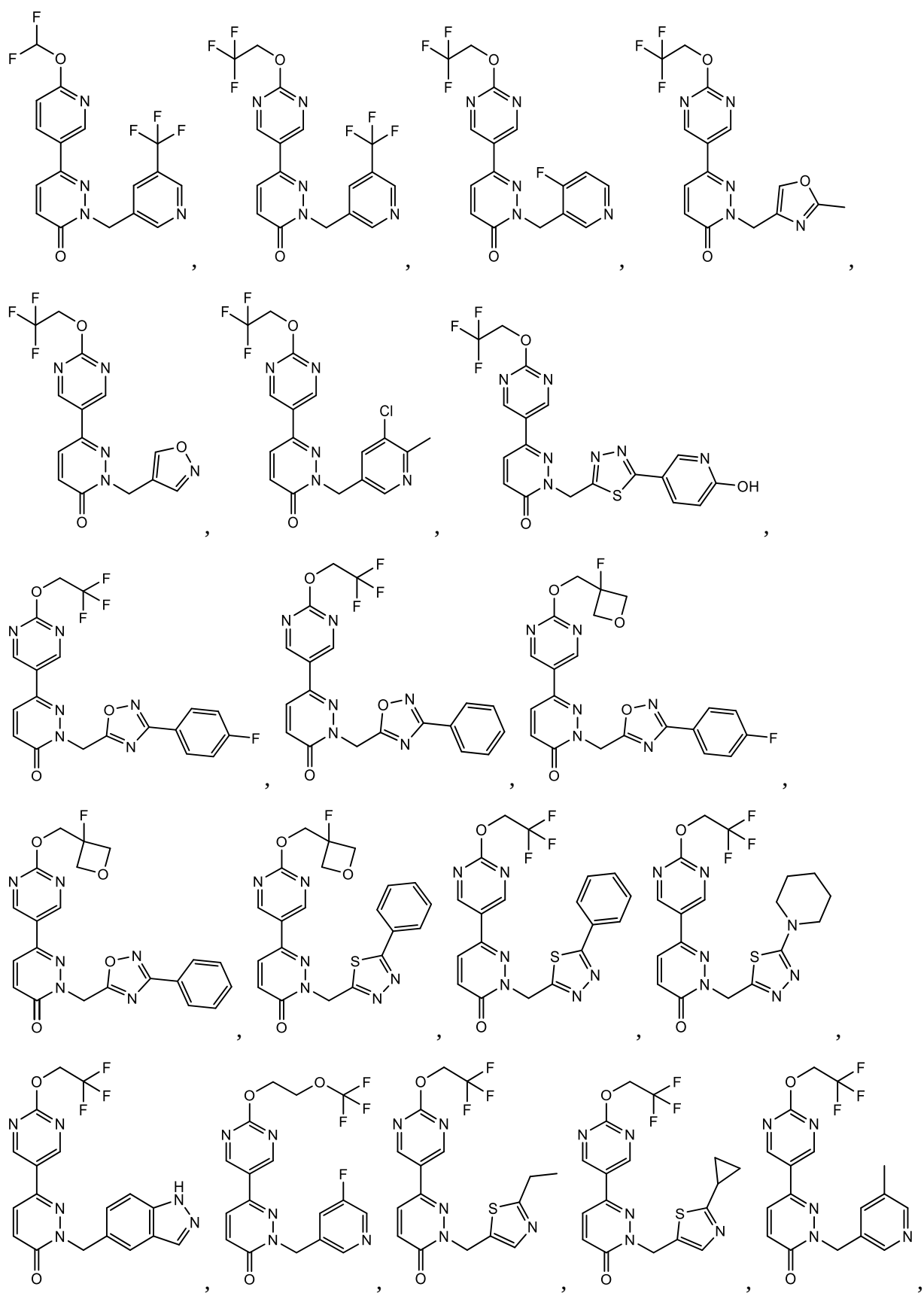
17. The compound of claim 1, selected from:

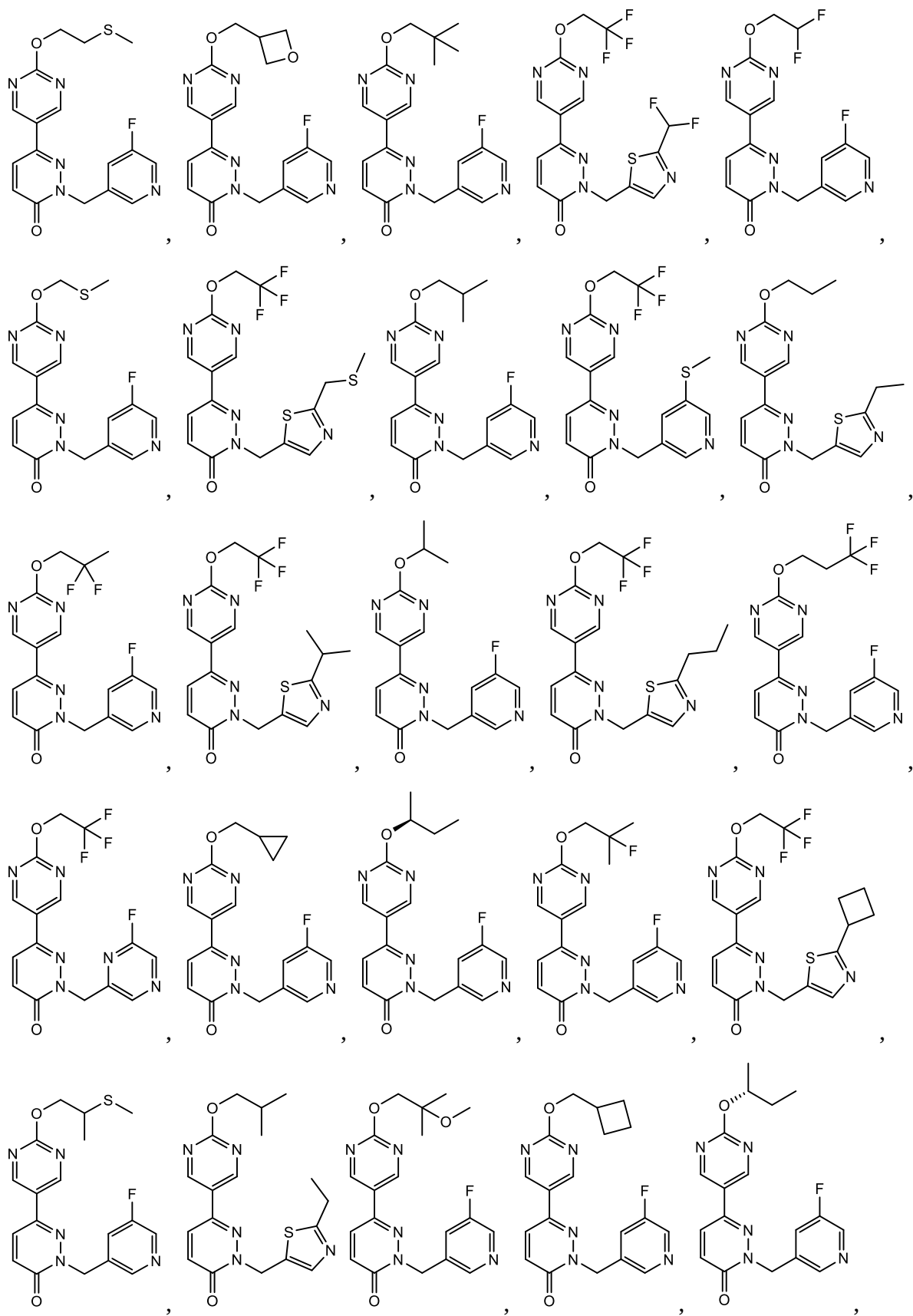


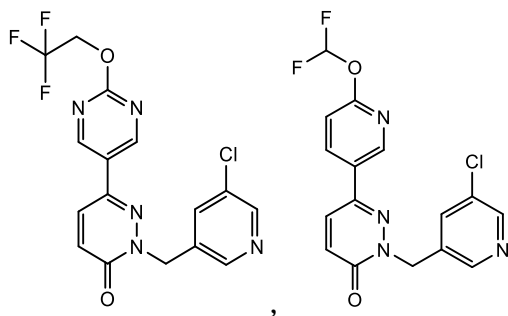
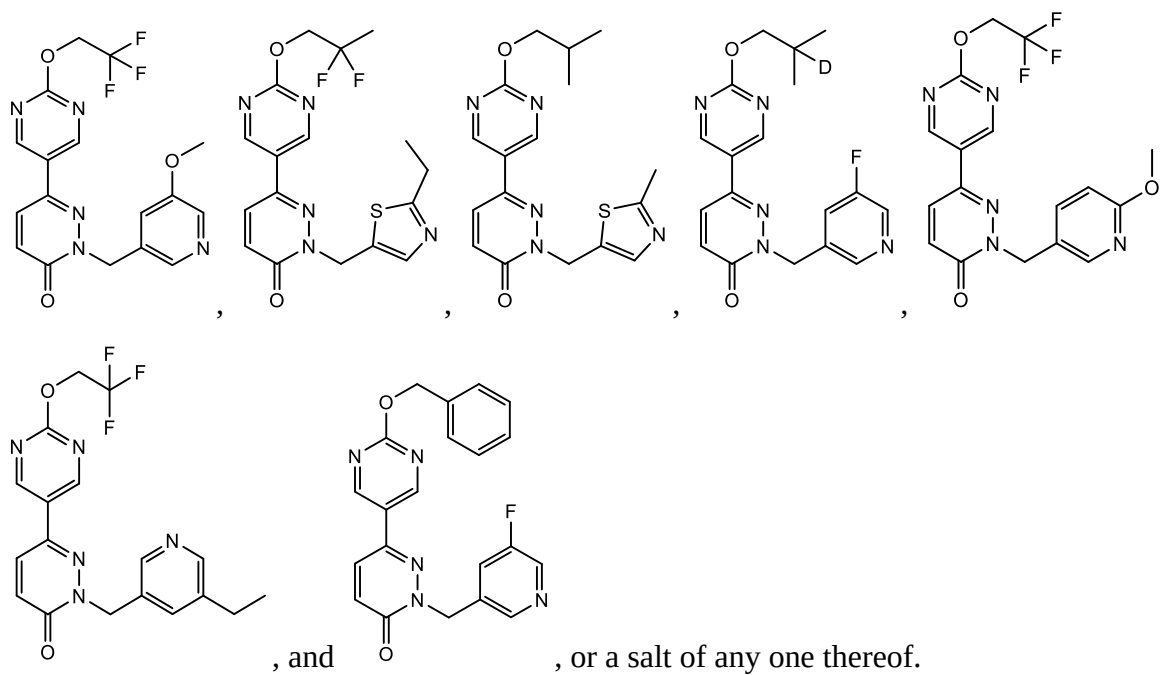




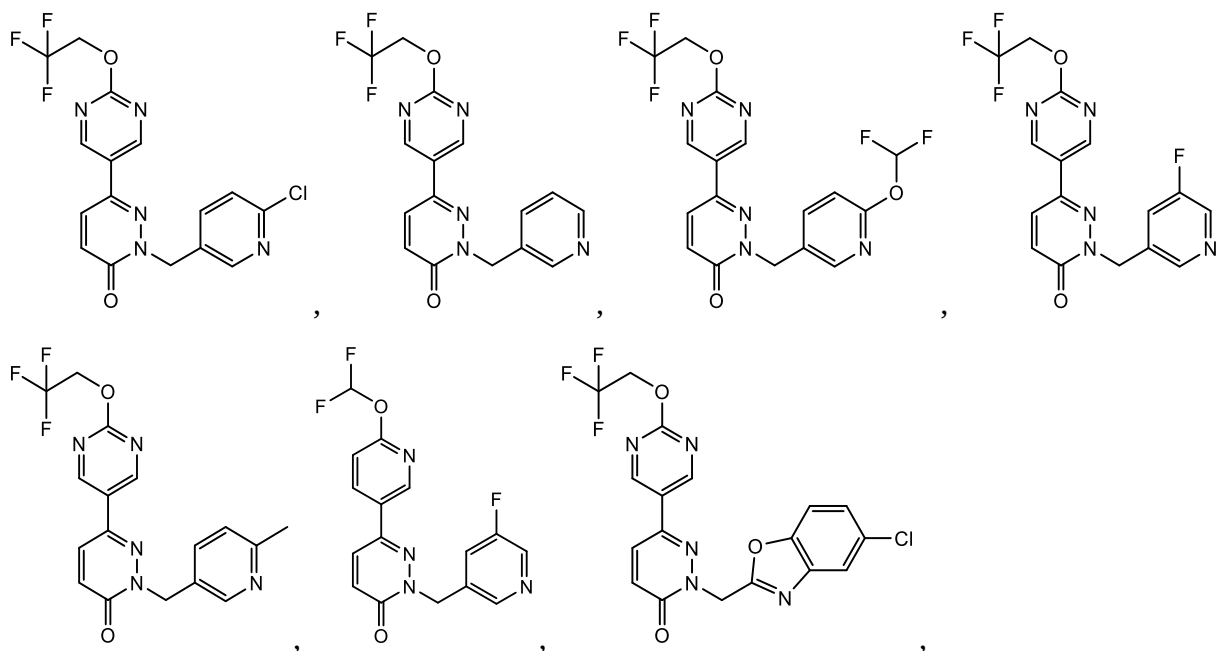


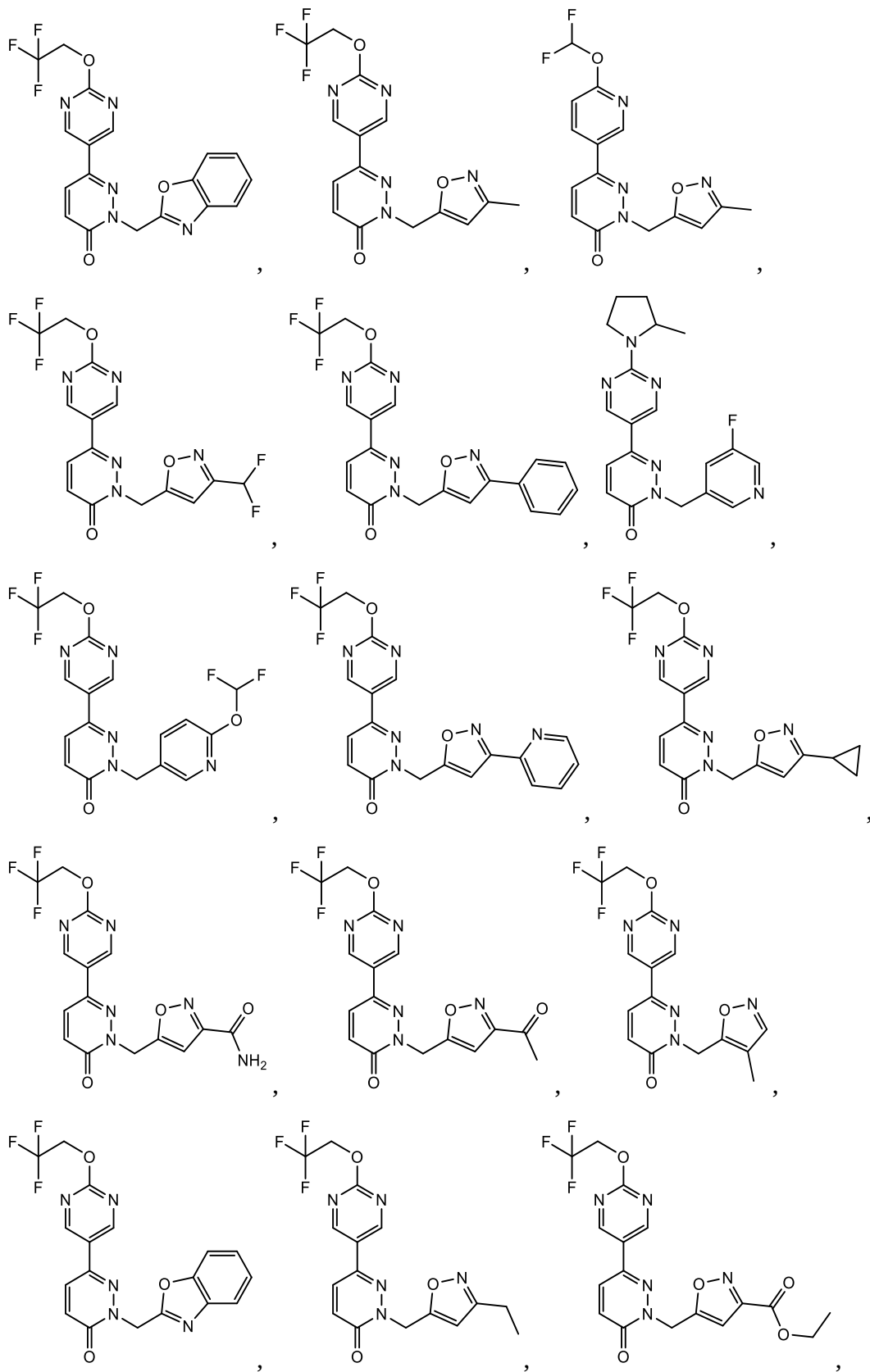


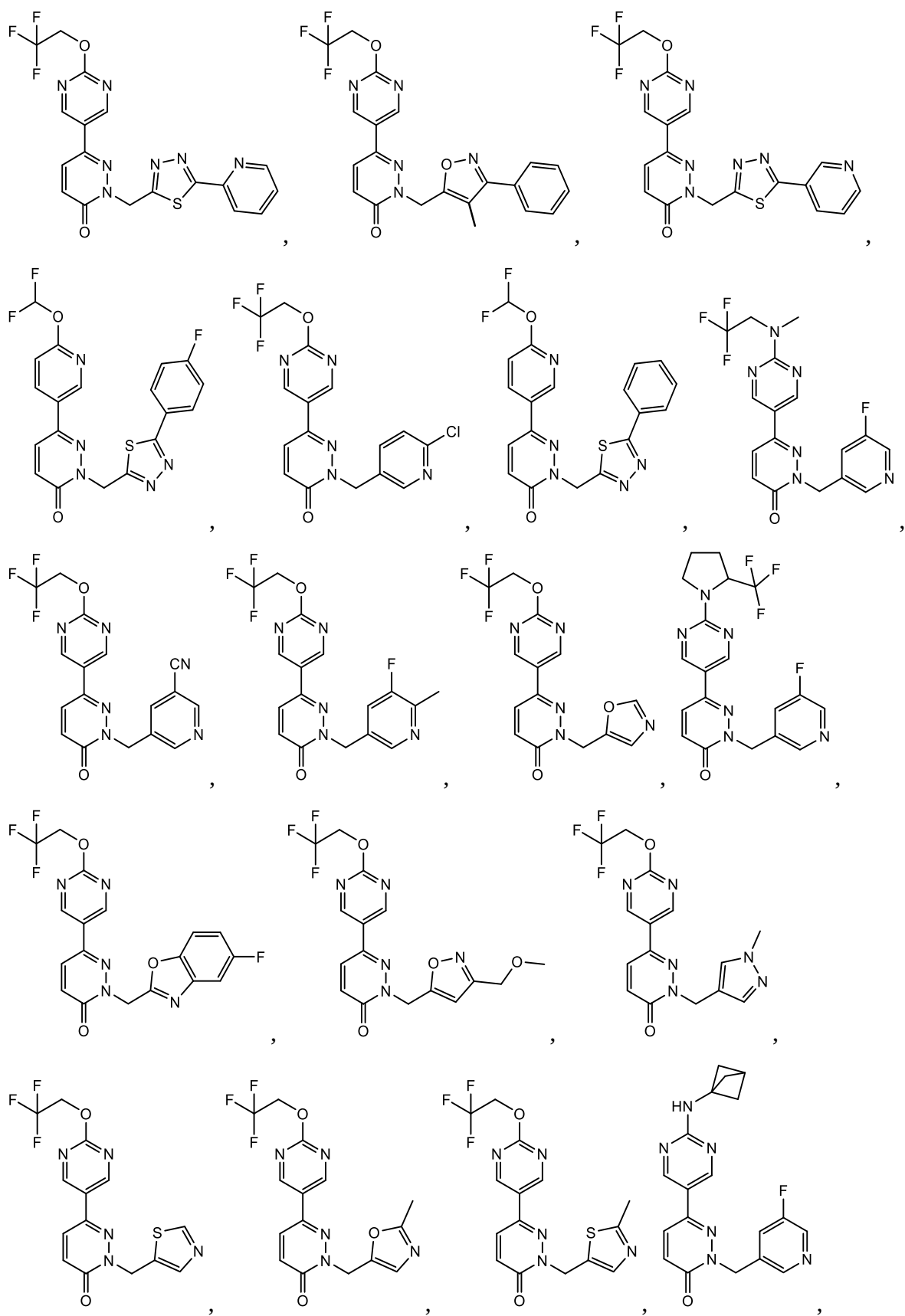


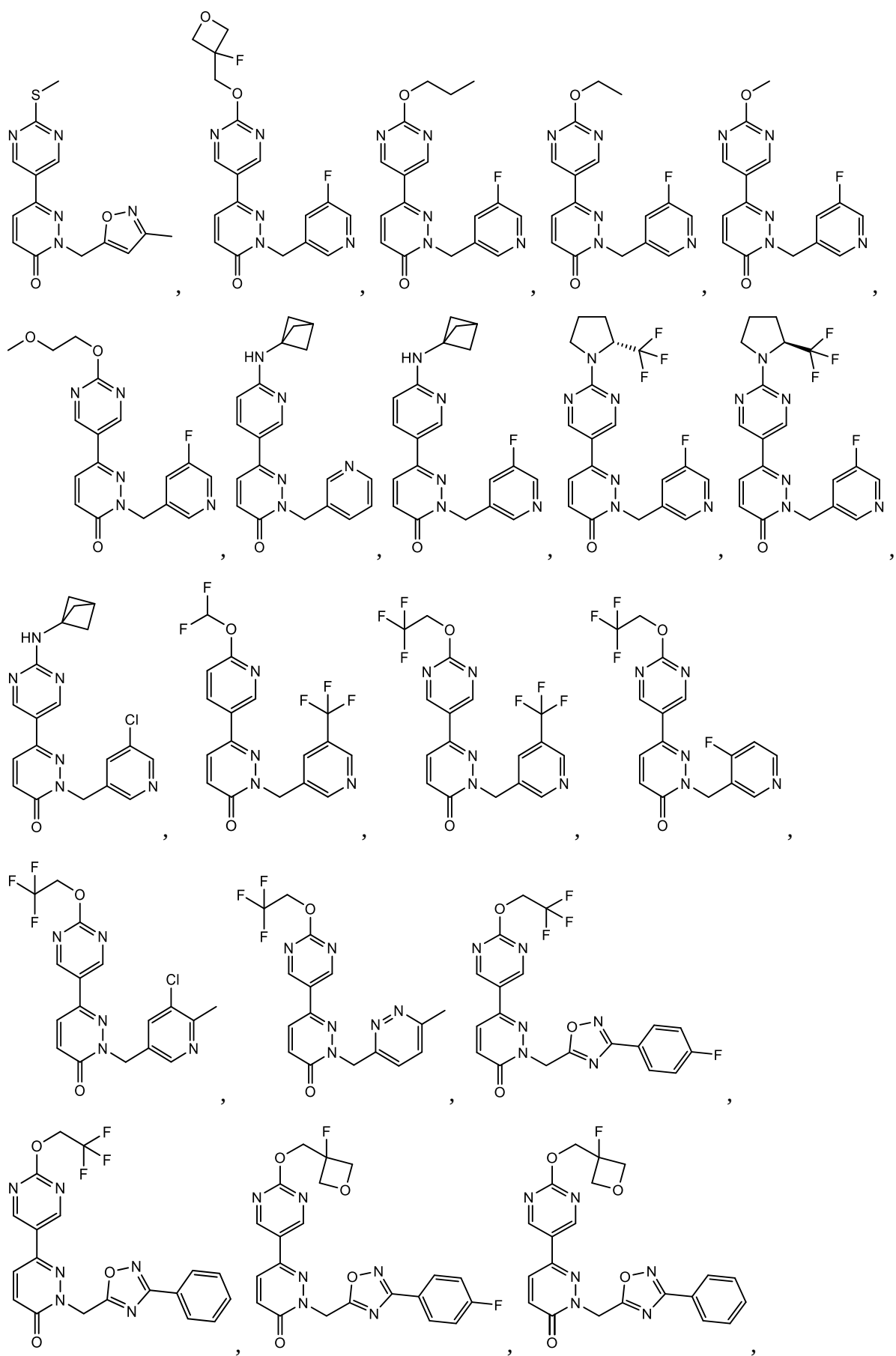


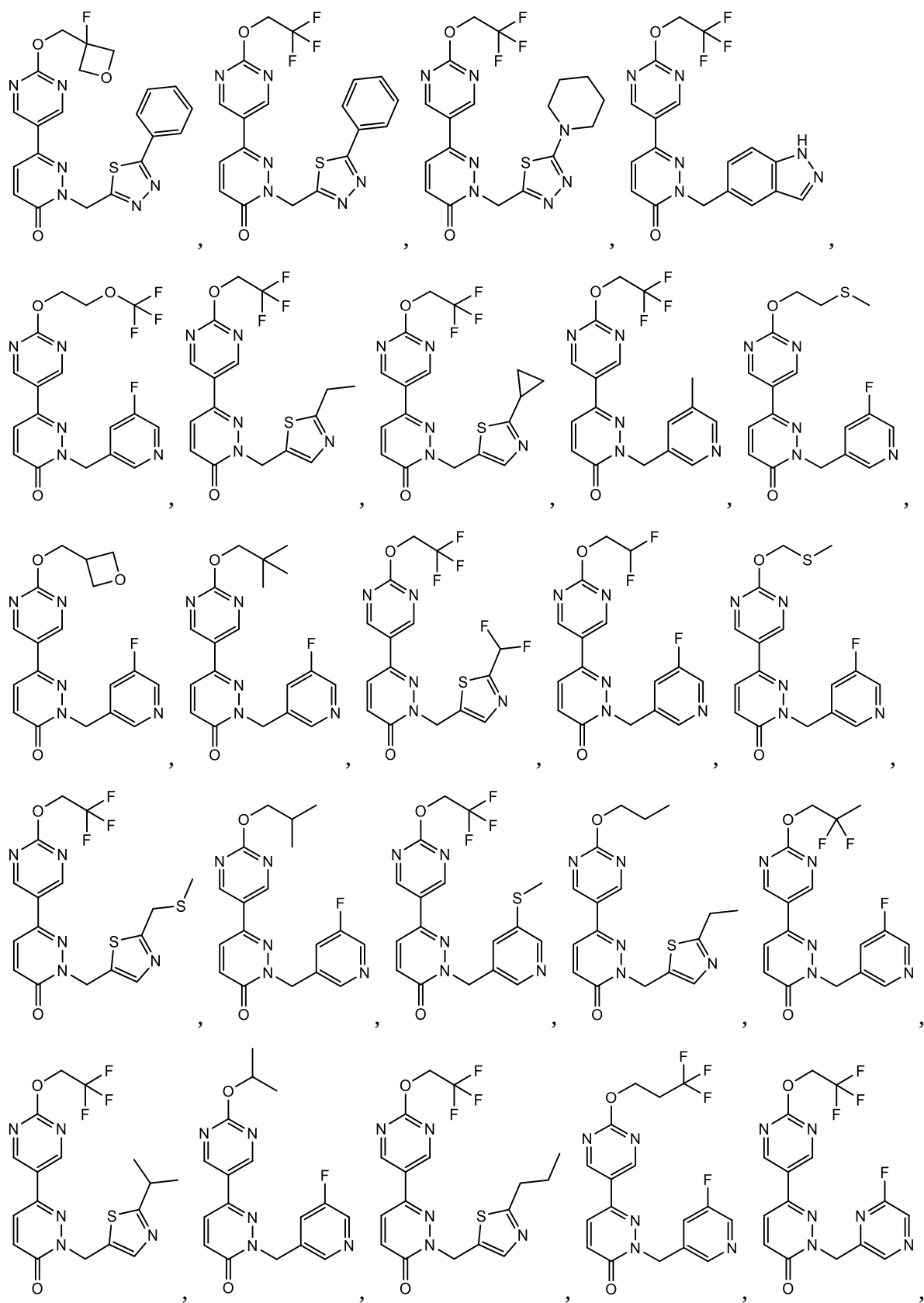
18. The compound of claim 1, selected from:

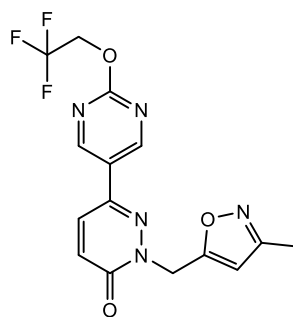
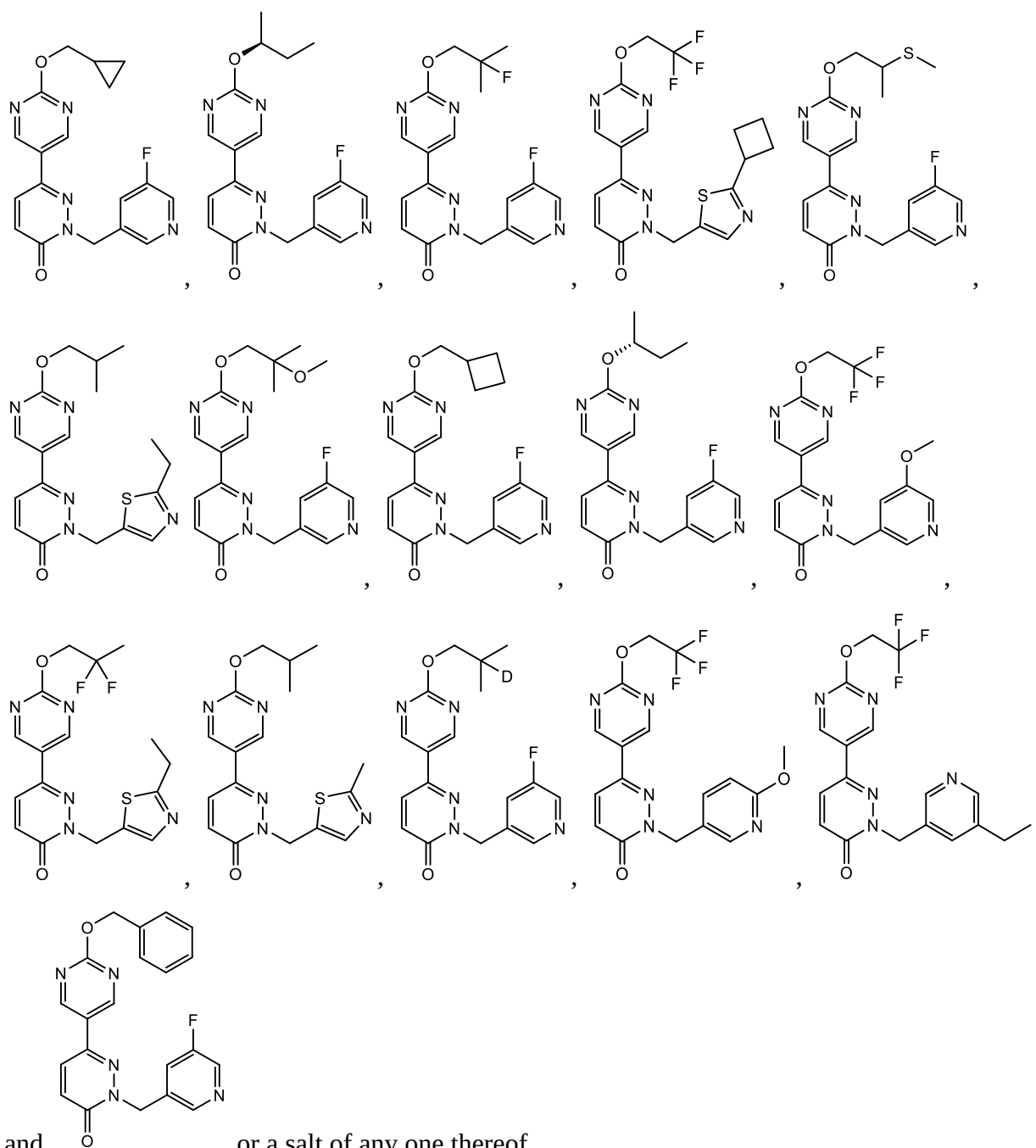






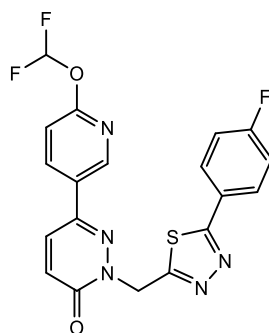




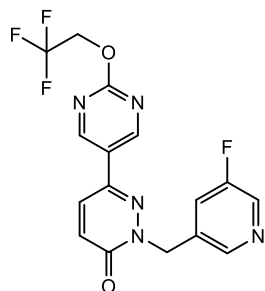


19. The compound of claim 1, selected from

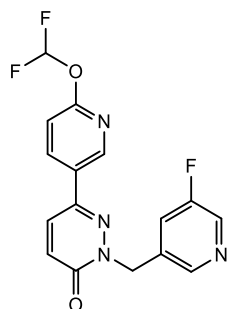
or a salt thereof.



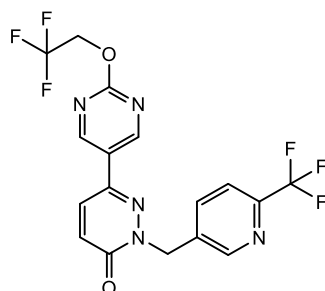
20. The compound of claim 1, selected from or a salt thereof.



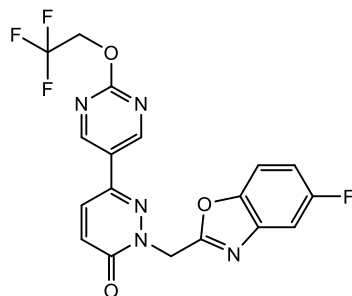
21. The compound of claim 1, selected from or a salt thereof.



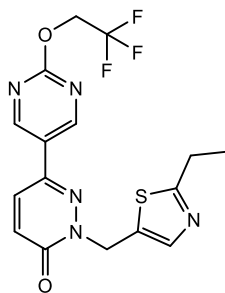
22. The compound of claim 1, selected from or a salt thereof.



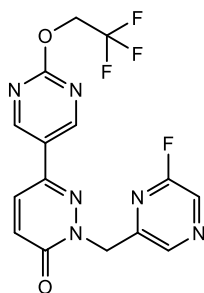
23. The compound of claim 1, selected from or a salt thereof.



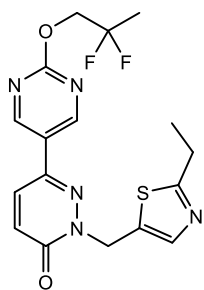
24. The compound of claim 1, selected from or a salt thereof.



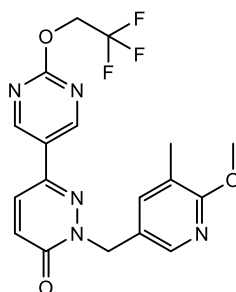
25. The compound of claim 1, selected from  or a salt thereof.



26. The compound of claim 1, selected from  or a salt thereof.

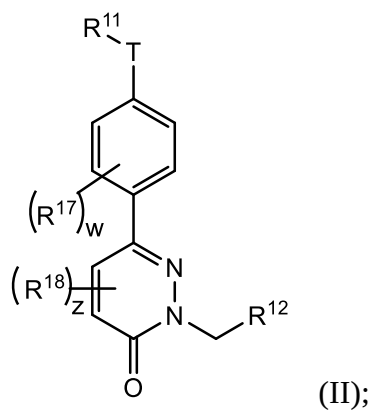


27. The compound of claim 1, selected from  or a salt thereof.



28. The compound of claim 1, selected from  or a salt thereof.

29. A compound represented by Formula (II):



or a salt thereof, wherein,

T is selected from -O-, -NR¹⁴-, -CR¹⁵R¹⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂;

R¹¹ is selected from:

C₁₋₅ haloalkyl optionally further substituted with one or more substituents independently selected from -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, =O, =S, -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R¹⁹;

R¹² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN; and when R¹² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O-;

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R¹⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more -R¹⁹;

R¹⁴ is selected from:

hydrogen, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁵ and R¹⁶ is independently selected from:

hydrogen, halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁷ and R¹⁸ is independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -NO₂, and -CN;

each R¹⁹ is independently selected from:

halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR²⁰, -SR²⁰, -N(R²⁰)₂, -C(O)R²⁰, -C(O)N(R²⁰)₂, -N(R²⁰)C(O)R²⁰, -N(R²⁰)C(O)N(R²⁰)₂, -OC(O)N(R²⁰)₂, -N(R²⁰)C(O)OR²⁰, -C(O)OR²⁰, -OC(O)R²⁰, -S(O)R²⁰, -S(O)₂R²⁰, -NO₂, =O, =S, =N(R²⁰), and -CN;

each R²⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

w is 0, 1, or 2; and

z is 0, 1, or 2.

30. The compound or salt of claim 29, wherein T is -O-.

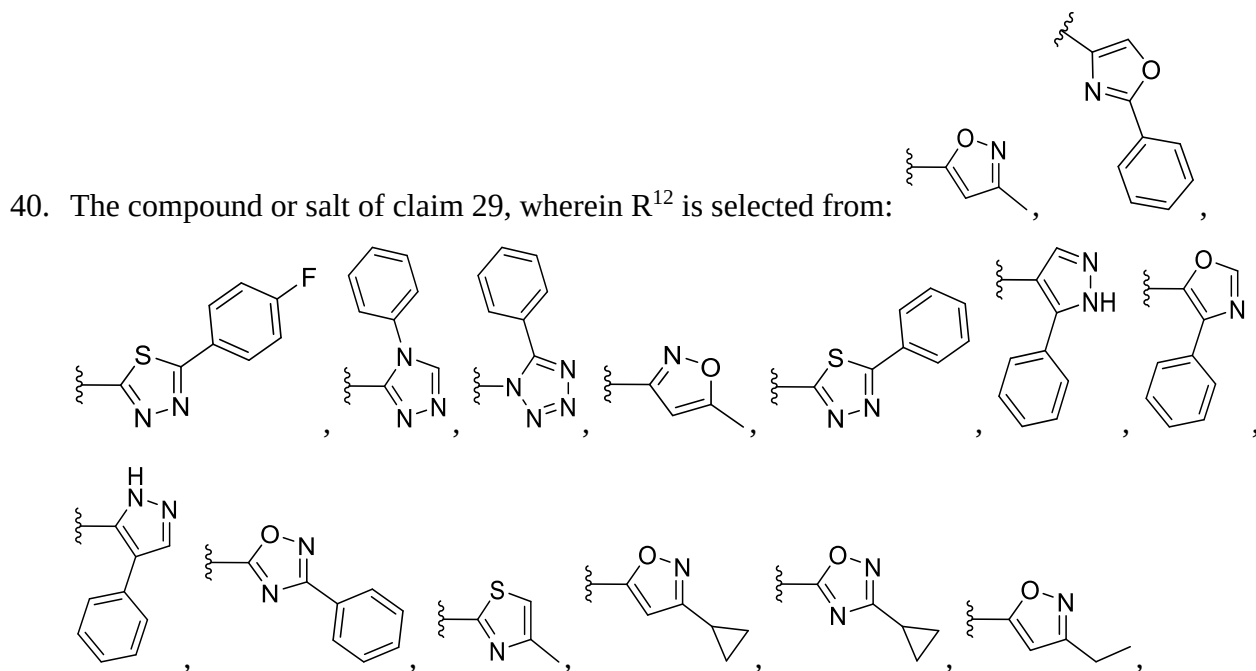
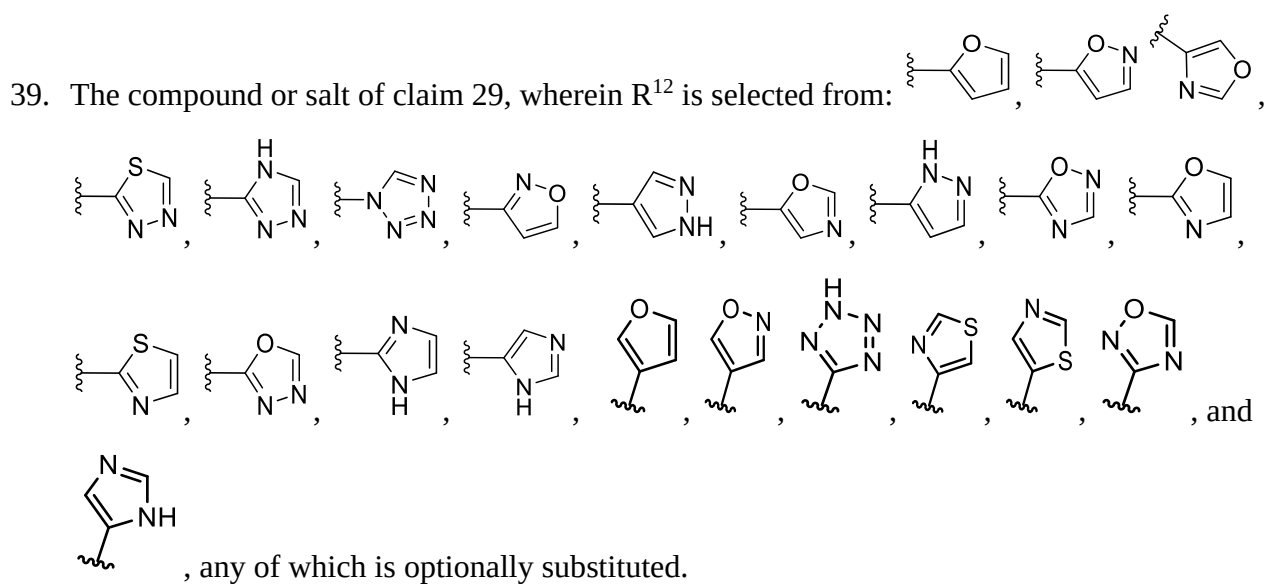
31. The compound or salt of claim 29, wherein R¹¹ is selected from C₁₋₃ haloalkyl optionally further substituted with one or more substituents independently selected from -OR²⁰, -SR²⁰, -N(R²⁰)₂, =O, -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle.

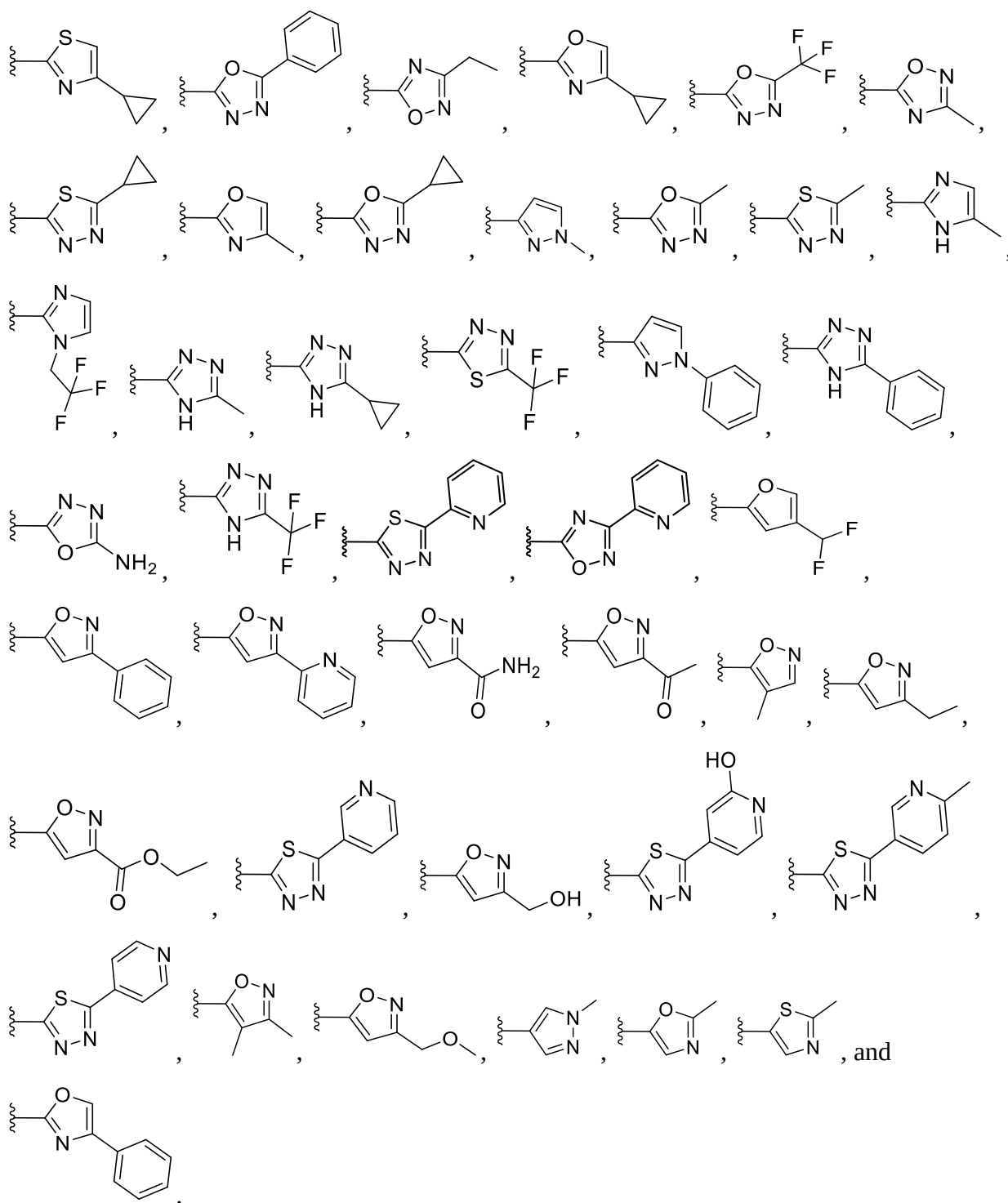
32. The compound or salt of claim 29, wherein R¹¹ is selected from -CHF₂ and -CH₂CF₃.

33. The compound or salt of claim 29, wherein R¹² is selected from optionally substituted 5- or 6-membered monocyclic heteroaryl and optionally substituted 9-membered bicyclic heteroaryl.

34. The compound or salt of claim 29, wherein R¹² is selected from isoxazole, oxazole, thiadiazole, triazole, isothiazole, tetrazole, pyrazole, pyrrole, furan, imidazole, oxadiazole, thiazole, pyridine, pyridazine, pyrimidine, pyrazine, tetrazine, benzoxazole, benzothiazole, benzimidazole, indole, indazole, and imidazopyridine, any of which is optionally substituted.

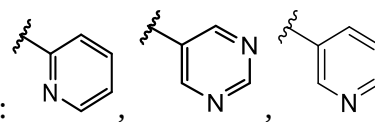
35. The compound or salt of claim 29, wherein R^{12} is not substituted at either ortho position on R^{12} relative to the point of connectivity to the rest of the molecule.
36. The compound or salt of claim 29, wherein R^{12} is not substituted at either ortho position on R^{12} with a carbocycle or heterocycle.
37. The compound or salt of claim 29, wherein R^{12} is selected from optionally substituted 5-membered heteroaryl.
38. The compound or salt of claim 29, wherein R^{12} is selected from isoxazole, oxazole, thiadiazole, oxadiazole, pyrazole, tetrazole, and thiazole, any of which is optionally substituted.





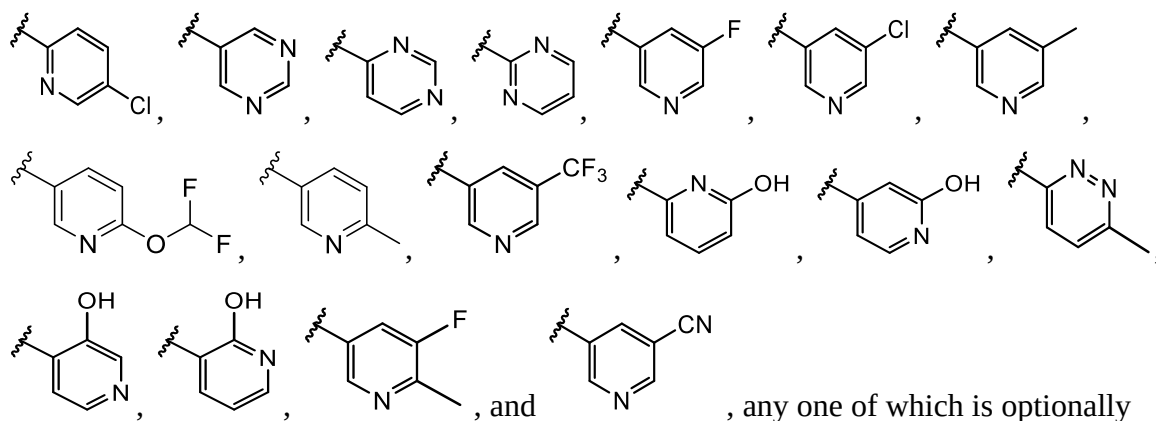
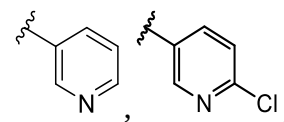
41. The compound or salt of claim 29, wherein R¹² is selected from optionally substituted 6-membered heteroaryl.
42. The compound or salt of claim 29, wherein R¹² is selected from pyridine and pyrimidine, any of which is optionally substituted.

43. The compound or salt of claim 29, wherein R¹² is selected from:
any of which is optionally substituted.



44. The compound or salt of claim 29, wherein R¹² is selected from optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyridyl N-oxide, optionally substituted pyridazine, and optionally substituted pyrimidyl N-oxide.

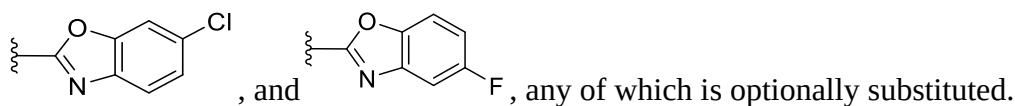
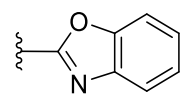
45. The compound or salt of claim 29, wherein R¹² is selected from:

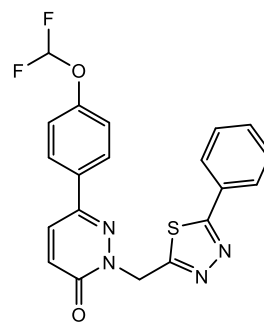


46. The compound or salt of claim 29, wherein R¹² is selected from optionally substituted bicyclic heteroaryl.

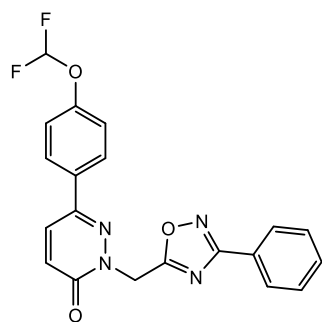
47. The compound or salt of claim 29, wherein R¹² is selected from optionally substituted benzoxazole.

48. The compound or salt of claim 29, wherein R¹² is selected from:

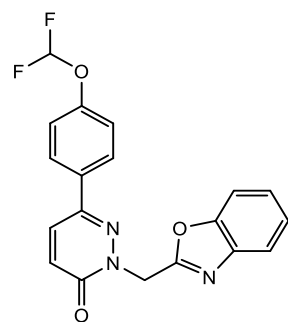




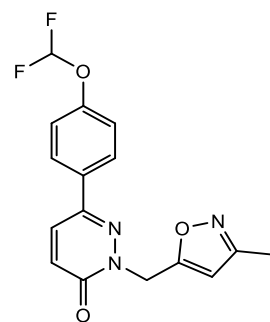
49. The compound or salt of claim 29, selected from:



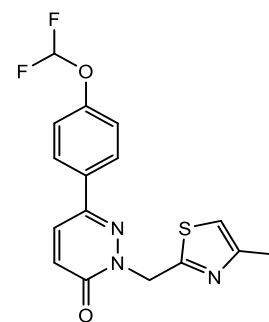
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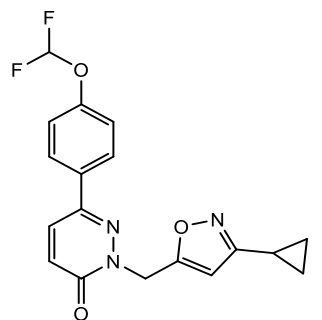
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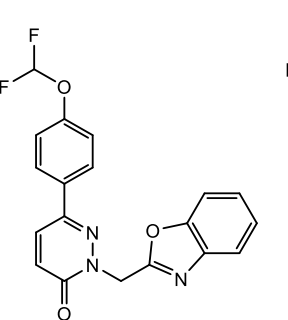
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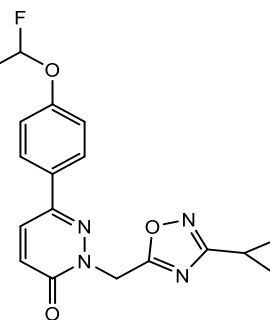
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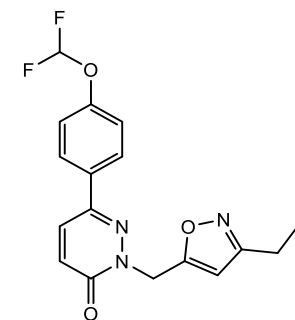
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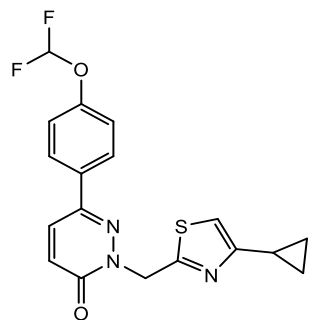
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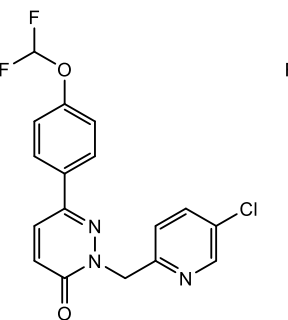
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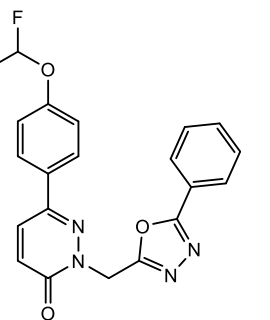
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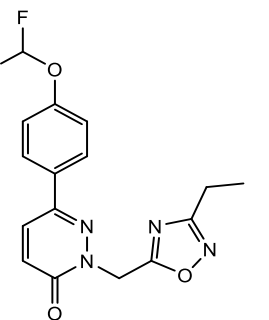
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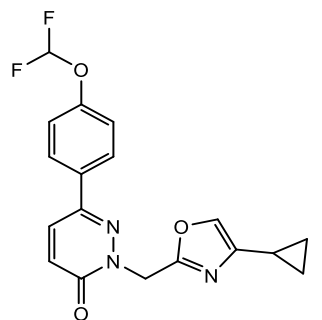
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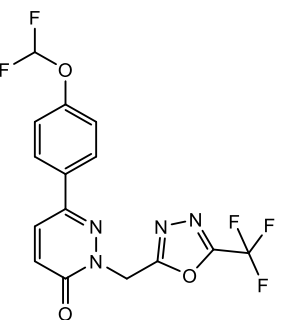
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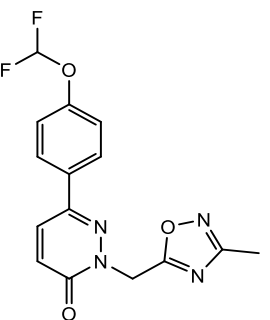
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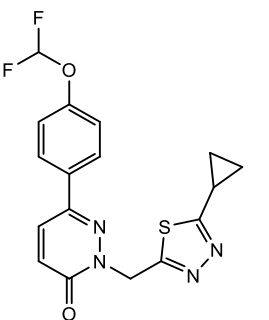
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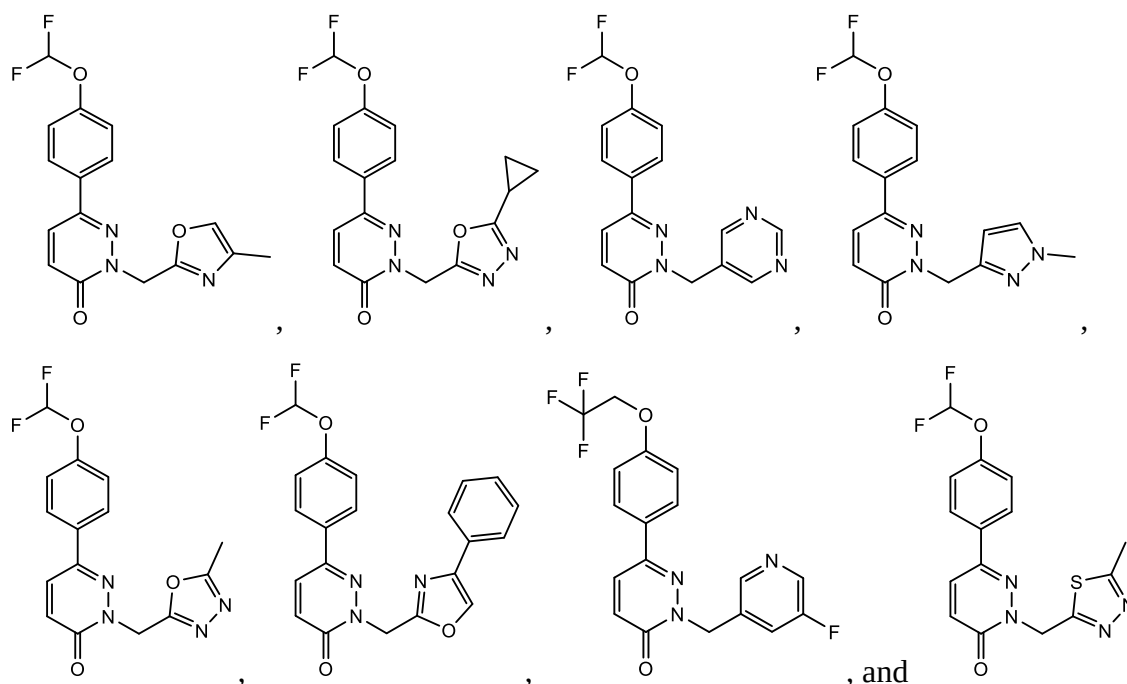
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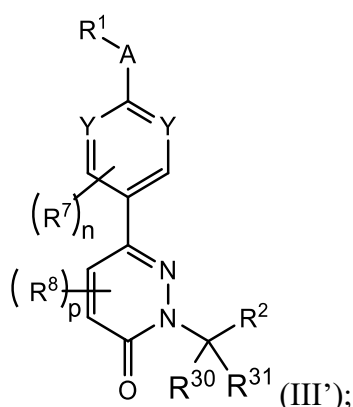


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50. A pharmaceutical composition comprising a compound or salt of any one of claims 1 to 49 and a pharmaceutically acceptable excipient.

51. Use of a compound or salt of Formula (III'):



or a salt thereof, in the manufacture of a medicament for treating activity-induced muscle damage, a neuromuscular condition, or a movement disorder, wherein:

each Y is independently selected from C(R³), N, and N⁺(-O⁻);

A is absent or selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S,

=N(R¹⁰), -CN, C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, wherein the C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; or

R¹ together with R³ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁵ form a 3- to 10- membered heterocycle or saturated C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or saturated C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹; or R¹ together with R⁴ form a 3- to 10- membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R⁹; and

when A is -NR⁴-, R¹ is additionally selected from hydrogen, and when A is -C(O)-, R¹ is additionally selected from -N(R¹⁰)₂ and -OR¹⁰;

when A is absent R¹ is further selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, and -CN;

R² is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN; and when R² is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from -O-;

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN, C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, wherein the C₃₋₁₀

carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more R⁹;

each R³, R⁵, and R⁶ is independently selected from:

hydrogen, halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or

R³ together with R¹ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; R⁵ together with R¹ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹;

R⁴ is independently selected from:

hydrogen; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or R⁴ together with R¹ form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

each R⁷ and R⁸ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

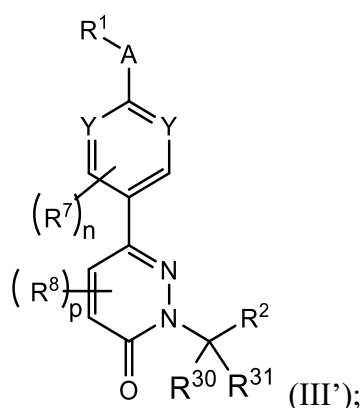
C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

R³⁰ and R³¹ are independently selected from R¹⁰ or R³⁰ and R³¹ come together to form a C₃₋₇ carbocycle, wherein the 3- to 7- membered heterocycle, wherein C₃₋₇ carbocycle and 3- to 7-membered heterocycle are optionally substituted with R⁹;

n is 0, 1, or 2; and

p is 0, 1, or 2.

52. A compound or salt of Formula (III'):



or a salt thereof, for use in treating activity-induced muscle damage, a neuromuscular condition, or a movement disorder, wherein:

each Y is independently selected from C(R³), N, and N⁺(-O⁻);

A is absent or selected from -O-, -NR⁴-, -CR⁵R⁶-, -C(O)-, -S-, -S(O)-, and -S(O)₂-;

R¹ is selected from:

C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -

$\text{N(R}^{10}\text{)C(O)OR}^{10}$, $-\text{C(O)OR}^{10}$, $-\text{OC(O)R}^{10}$, $-\text{S(O)R}^{10}$, $-\text{S(O)}_2\text{R}^{10}$, $-\text{NO}_2$, $=\text{O}$, $=\text{S}$, $=\text{N(R}^{10}\text{)}$, $-\text{CN}$, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R^9 ; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-\text{OR}^{10}$, $-\text{SR}^{10}$, $-\text{N(R}^{10}\text{)}_2$, $-\text{C(O)R}^{10}$, $-\text{C(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)R}^{10}$, $-\text{N(R}^{10}\text{)C(O)N(R}^{10}\text{)}_2$, $-\text{OC(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)OR}^{10}$, $-\text{C(O)OR}^{10}$, $-\text{OC(O)R}^{10}$, $-\text{S(O)R}^{10}$, $-\text{S(O)}_2\text{R}^{10}$, $-\text{NO}_2$, $=\text{O}$, $=\text{S}$, $=\text{N(R}^{10}\text{)}$, and $-\text{CN}$; or

R^1 together with R^3 form a 5- to 10- membered heterocycle or C_{5-10} carbocycle, wherein the 5- to 10- membered heterocycle or C_{5-10} carbocycle is optionally substituted with one or more R^9 ; or R^1 together with R^5 form a 3- to 10- membered heterocycle or saturated C_{3-10} carbocycle, wherein the 3- to 10- membered heterocycle or saturated C_{3-10} carbocycle is optionally substituted with one or more R^9 ; or R^1 together with R^4 form a 3- to 10- membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R^9 ; and

when A is $-\text{NR}^4-$, R^1 is additionally selected from hydrogen, and when A is $-\text{C(O)-}$, R^1 is additionally selected from $-\text{N(R}^{10}\text{)}_2$ and $-\text{OR}^{10}$;

when A is absent R^1 is further selected from halogen, $-\text{OR}^{10}$, $-\text{SR}^{10}$, $-\text{N(R}^{10}\text{)}_2$, $-\text{C(O)R}^{10}$, $-\text{C(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)R}^{10}$, $-\text{N(R}^{10}\text{)C(O)N(R}^{10}\text{)}_2$, $-\text{OC(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)OR}^{10}$, $-\text{C(O)OR}^{10}$, $-\text{OC(O)R}^{10}$, $-\text{S(O)R}^{10}$, $-\text{S(O)}_2\text{R}^{10}$, $-\text{NO}_2$, and $-\text{CN}$;

R^2 is a heteroaryl optionally substituted with one or more substituents independently selected from:

halogen, $-\text{OR}^{10}$, $-\text{SR}^{10}$, $-\text{N(R}^{10}\text{)}_2$, $-\text{C(O)R}^{10}$, $-\text{C(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)R}^{10}$, $-\text{N(R}^{10}\text{)C(O)N(R}^{10}\text{)}_2$, $-\text{OC(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)OR}^{10}$, $-\text{C(O)OR}^{10}$, $-\text{OC(O)R}^{10}$, $-\text{S(O)R}^{10}$, $-\text{S(O)}_2\text{R}^{10}$, $-\text{NO}_2$, $=\text{O}$, $=\text{S}$, $=\text{N(R}^{10}\text{)}$, and $-\text{CN}$; and when R^2 is pyridyl or pyrimidyl, a substituent on a nitrogen atom of the pyridyl or pyrimidyl is optionally further selected from $-\text{O}-$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-\text{OR}^{10}$, $-\text{SR}^{10}$, $-\text{N(R}^{10}\text{)}_2$, $-\text{C(O)R}^{10}$, $-\text{C(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)R}^{10}$, $-\text{N(R}^{10}\text{)C(O)N(R}^{10}\text{)}_2$, $-\text{OC(O)N(R}^{10}\text{)}_2$, $-\text{N(R}^{10}\text{)C(O)OR}^{10}$, $-\text{C(O)OR}^{10}$, $-\text{OC(O)R}^{10}$, $-\text{S(O)R}^{10}$, $-\text{S(O)}_2\text{R}^{10}$, $-\text{NO}_2$, $=\text{O}$, $=\text{S}$, $=\text{N(R}^{10}\text{)}$, $-\text{CN}$, C_{3-10} carbocycle and 3- to 10-membered heterocycle, wherein the C_{3-10}

carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more R⁹; and

C₃₋₁₀ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more R⁹;

each R³, R⁵, and R⁶ is independently selected from:

hydrogen, halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or

R³ together with R¹ form a 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle, wherein the 5- to 10- membered heterocycle or C₅₋₁₀ carbocycle is optionally substituted with one or more R⁹; R⁵ together with R¹ form a 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle, wherein the 3- to 10- membered heterocycle or C₃₋₁₀ carbocycle is optionally substituted with one or more R⁹;

R⁴ is independently selected from:

hydrogen; and

C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN; or R⁴ together with R¹ form a 3- to 10-membered heterocycle, which is optionally substituted with one or more R⁹;

each R⁷ and R⁸ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, -CN, and C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -NO₂, and -CN;

each R⁹ is independently selected from:

halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), -CN; and

C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR¹⁰, -SR¹⁰, -N(R¹⁰)₂, -C(O)R¹⁰, -C(O)N(R¹⁰)₂, -N(R¹⁰)C(O)R¹⁰, -N(R¹⁰)C(O)N(R¹⁰)₂, -OC(O)N(R¹⁰)₂, -N(R¹⁰)C(O)OR¹⁰, -C(O)OR¹⁰, -OC(O)R¹⁰, -S(O)R¹⁰, -S(O)₂R¹⁰, -NO₂, =O, =S, =N(R¹⁰), and -CN;

each R¹⁰ is independently selected from:

hydrogen; and

C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle; and

C₃₋₁₀ carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO₂, -NH₂, =O, =S, -O-C₁₋₆ alkyl, -S-C₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, -NH(C₁₋₆ alkyl), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ carbocycle, 3- to 10-membered heterocycle, and haloalkyl;

R³⁰ and R³¹ are independently selected from R¹⁰ or R³⁰ and R³¹ come together to form a C₃₋₇ carbocycle, wherein the 3- to 7- membered heterocycle, wherein C₃₋₇ carbocycle and 3- to 7-membered heterocycle are optionally substituted with R⁹;

n is 0, 1, or 2; and

p is 0, 1, or 2.

53. The use of claim 51, or the compound for use of claim 52, wherein each R³⁰ and R³¹ is independently hydrogen.
54. The use of claim 51, or the compound for use of claim 52, wherein A is absent.
55. The use of claim 51, or the compound for use of claim 52, wherein at least one Y is N or N⁺(-O⁻).
56. The use of claim 51, or the compound for use of claim 52, wherein one Y is N and one Y is C(R³).
57. The use of claim 51, or the compound for use of claim 52, wherein one Y is N⁺(-O⁻) and one Y is C(R³).
58. The use of claim 51, or the compound for use of claim 52, wherein one Y is N and one Y is N⁺(-O⁻).
59. The use of claim 51, or the compound for use of claim 52, wherein each Y is N.
60. The use of claim 51, or the compound for use of claim 52, wherein each Y is C(R³).
61. The use of claim 51, or the compound for use of claim 52, wherein the neuromuscular condition is selected from Duchenne muscular dystrophy, Becker muscular dystrophy, myotonic dystrophy 1, myotonic dystrophy 2, facioscapulohumeral muscular dystrophy, oculopharyngeal muscular dystrophy, limb girdle muscular dystrophy, tendinitis, carpal tunnel syndrome.

62. The use or compound for use of claim 61, wherein the neuromuscular condition is Duchenne muscular dystrophy.
63. The use or compound for use of claim 61, wherein the neuromuscular condition is Becker muscular dystrophy.
64. The use of claim 51, or the compound for use of claim 52, wherein the movement disorder comprises muscle spasticity.
65. The use or compound for use of claim 64, wherein the muscle spasticity is selected from spasticity associated with multiple sclerosis, Parkinson's disease, Alzheimer's disease, or cerebral palsy, or injury, or a traumatic event such as stroke, traumatic brain injury, spinal cord injury, hypoxia, meningitis, encephalitis, phenylketonuria, or amyotrophic lateral sclerosis.
66. The use of claim 51, or the compound for use of claim 52, wherein the compound or salt is to be administered in an amount sufficient to reduce involuntary muscle contractions.
67. The use or compound for use of claim 66, wherein the compound or salt is to be administered in an amount sufficient to reduce involuntary muscle contractions by at least 10%.
68. The use of claim 51, or the compound for use of claim 52, wherein an additional therapeutic agent is to be further administered.
69. The use or compound for use of claim 68, wherein the additional therapeutic agent is corticosteroid.
70. The use or compound for use of claim 69, wherein the corticosteroid is deflazacort or prednisone.
71. The use or compound for use of claim 68, wherein the additional therapeutic agent is vamorolone.
72. The use or compound for use of claim 68, wherein the additional therapeutic agent is a gene therapy.
73. The use or compound for use of claim 72, wherein the gene therapy comprises dystrophin gene or a variant or truncated version thereof.
74. The use or compound for use of claim 72, wherein the gene therapy comprises microdystrophin.
75. The use or compound for use of claim 68, wherein the additional therapeutic agent is eteplirsen.
76. The use or compound for use of claim 68, wherein the additional therapeutic agent is ataluren.