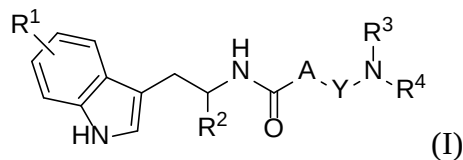


Claims

1. A compound of Formula (I):



wherein

R¹ is H, halo, C₁-₄alkyl, or CF₃;

R² is -CF₃ or C₁-₄alkyl unsubstituted or substituted with halo or -CF₃;

A is a 5-membered heteroaryl ring;

Y is absent or is C₁-₄alkylene;

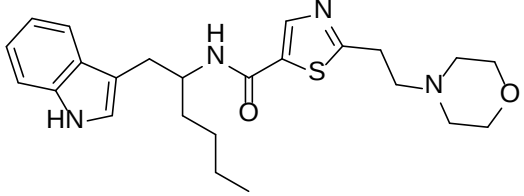
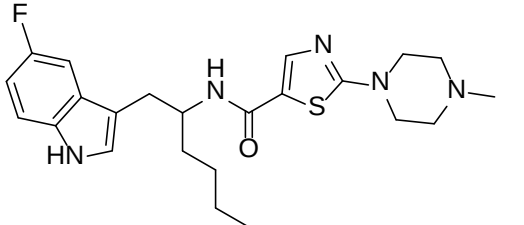
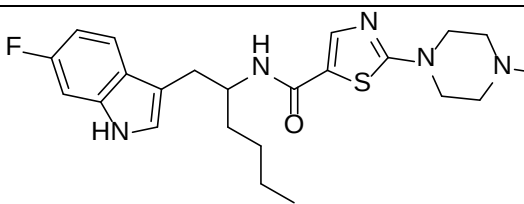
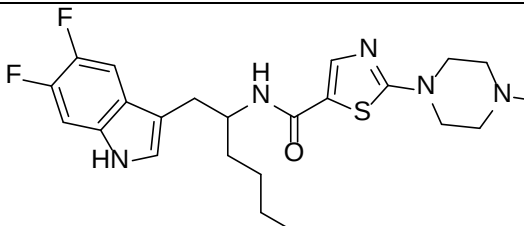
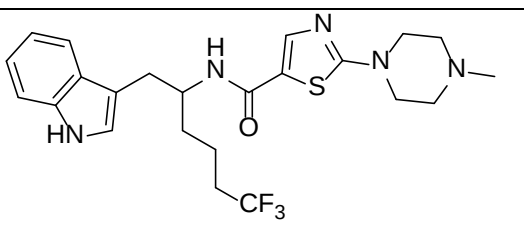
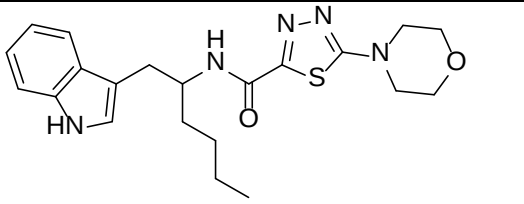
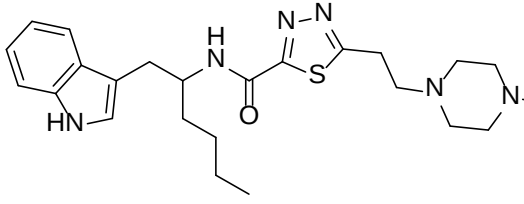
Where when Y is absent ~~or is C₁-₄alkylene~~, R³ and R⁴ taken together with the nitrogen to which they are attached form a monocyclic heterocycloalkyl ring, unsubstituted or substituted with C₁-₄alkyl; ~~or and~~

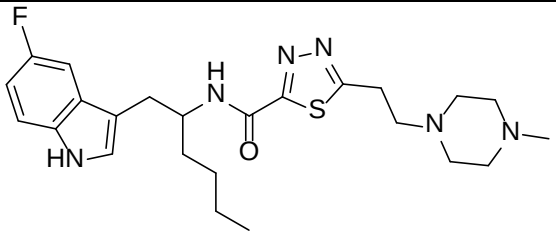
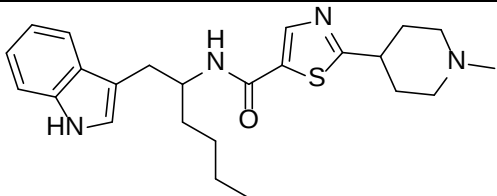
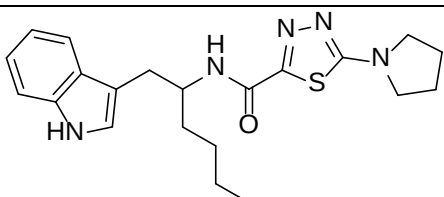
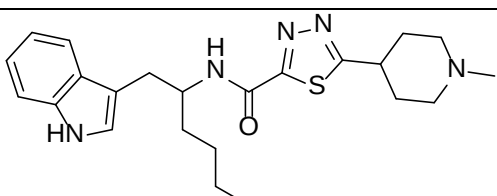
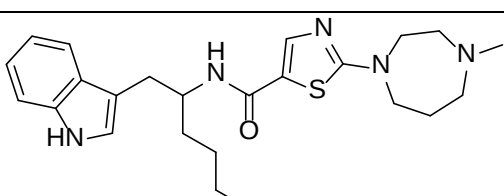
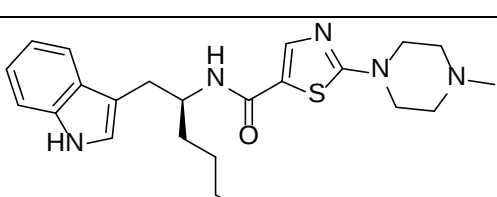
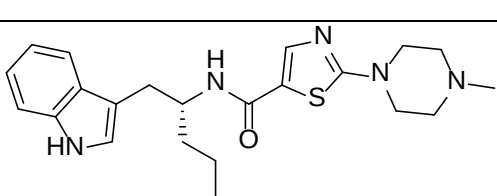
~~where~~when Y is C₁-₄alkylene, R³ and R⁴ taken together with the nitrogen to which they are attached form a monocyclic heterocycloalkyl ring, unsubstituted or substituted with C₁-₄alkyl; or R³ and Y taken together with the nitrogen to which R³ is attached form a monocyclic heterocycloalkyl ring, and R⁴ is H or C₁-₄alkyl;
or a pharmaceutically acceptable salt thereof.

2. A compound selected from the group consisting of:

	N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide
	N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(piperazin-1-yl)thiazole-5-carboxamide
	N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(2-(4-methylpiperazin-1-yl)ethyl)thiazole-5-carboxamide

	N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)oxazole-5-carboxamide
	N-(1-(1H-Indol-3-yl)hexan-2-yl)-5-(4-methylpiperazin-1-yl)-1,3,4-thiadiazole-2-carboxamide
	N-(1-(1H-Indol-3-yl)hexan-2-yl)-5-(4-methylpiperazin-1-yl)-4H-1,2,4-triazole-3-carboxamide
	N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)-1H-imidazole-5-carboxamide
	N-(1-(5-Fluoro-1H-indol-3-yl)hexan-2-yl)-2-(2-morpholinoethyl)thiazole-5-carboxamide
	N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-morpholinothiazole-5-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-2-(pyrrolidin-1-yl)thiazole-5-carboxamide

	N-(1-(1H-indol-3-yl)hexan-2-yl)-2-(2-morpholinoethyl)thiazole-5-carboxamide
	N-(1-(5-fluoro-1H-indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide
	N-(1-(6-fluoro-1H-indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide
	N-(1-(5,6-difluoro-1H-indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide
	2-(4-methylpiperazin-1-yl)-N-(6,6,6-trifluoro-1-(1H-indol-3-yl)hexan-2-yl)thiazole-5-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-5-morpholino-1,3,4-thiadiazole-2-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-5-(2-(4-methylpiperazin-1-yl)ethyl)-1,3,4-thiadiazole-2-carboxamide

	N-(1-(5-fluoro-1H-indol-3-yl)hexan-2-yl)-5-(2-(4-methylpiperazin-1-yl)ethyl)-1,3,4-thiadiazole-2-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-2-(1-methylpiperidin-4-yl)thiazole-5-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-5-(pyrrolidin-1-yl)-1,3,4-thiadiazole-2-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-5-(1-methylpiperidin-4-yl)-1,3,4-thiadiazole-2-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-2-(4-methyl-1,4-diazepan-1-yl)thiazole-5-carboxamide
	(S)-N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide and
	(R)-N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide

and pharmaceutically acceptable salts thereof.

~~3. A pharmaceutical composition comprising (a) at least one compound or pharmaceutically acceptable salt thereof according to any one of claims 1-2 or 5-34, and (b) a pharmaceutically acceptable excipient.~~

~~4. A method of treating a disease or medical condition associated with protein aggregation, comprising administering to a subject in need of such treatment an effective amount of at least one compound or pharmaceutically acceptable salt thereof according to any one of claims 1-2 or 5-34.~~

~~5.3.~~ The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is H, fluoro, chloro, bromo, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, or tert-butyl.

~~6.4.~~ The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is H or fluoro.

~~7.5.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is -CF₃, or is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, or tert-butyl, each unsubstituted or substituted with fluoro, chloro, bromo, or -CF₃.

~~8.6.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is -CF₃ or is C₁₋₄alkyl optionally substituted with halo or -CF₃.

~~9.7.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is C₃₋₄alkyl, unsubstituted or substituted with fluoro or -CF₃.

~~10.8.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is butyl.

~~11.9.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is propyl substituted with -CF₃.

~~12.10.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is in an “R” stereochemical configuration.

~~13.11.~~ The compound of any one of claims 1 or ~~5-6 3-4~~, or a pharmaceutically acceptable salt thereof, wherein R² is in an “S” stereochemical configuration.

~~14.~~ The compound of any one of claims 1 or ~~5-6~~, wherein R^2 is substantially an “R” or substantially an “S” stereochemical configuration.

~~15.12.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof, wherein A is a 5-membered heteroaryl ring with two or three heteroatom ring atoms.

~~16.13.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof wherein A is a 5-membered heteroaryl ring with two non-adjacent heteroatom ring atoms.

~~17.14.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof, wherein A is thiazole, thiadiazole, oxazole, imidazole, or triazole.

~~18.15.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof, wherein A is ~~thiazole or~~ thiadiazole.

~~19.16.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof, wherein A is thiazole.

~~20.17.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof, wherein Y is absent.

~~21.18.~~ The compound of any one of claims 1 or ~~5-14 3-11~~, or a pharmaceutically acceptable salt thereof, wherein Y is $-CH_2-$, $-CH_2CH_2-$, $-CH(CH_3)-$, $-(CH_2)_3-$, $-C(CH_3)_2-$, $-(CH_2)_4-$, $-CH((CH_2)_2CH_3)-$, $-CH(CH(CH_3)_2)-$, $-CH(CH_2CH_3)CH_2-$, $-CH(CH_3)CH(CH_3)-$, $-CH(CH_3)(CH_2)_2-$, or $-CH_2CH(CH_3)CH_2-$.

~~22.19.~~ The compound of claim ~~21 18~~, or a pharmaceutically acceptable salt thereof, wherein Y is $-CH_2-$, $-CH_2CH_2-$, or $-CH(CH_3)-$.

~~23.20.~~ The compound of claim ~~21 18~~, or a pharmaceutically acceptable salt thereof, wherein Y is $-CH_2CH_2-$.

~~24.21.~~ The compound of any one of claims 1 or ~~5-23 3-20~~, or a pharmaceutically acceptable salt thereof, wherein R^3 and R^4 are taken together with the nitrogen to which they are attached form a monocyclic heterocycloalkyl ring, unsubstituted or substituted with C_{1-4} alkyl.

~~25.22.~~ The compound of claim ~~24 21~~, or a pharmaceutically acceptable salt thereof, wherein R³ and R⁴ taken together with the nitrogen to which they are attached form azetidine, pyrrolidine, piperidine, azepine, piperazine, morpholine, thiomorpholine, or 1,1-dioxo-thiomorpholine, each unsubstituted or substituted with C₁₋₄alkyl.

~~26.23.~~ The compound of claim ~~24 21~~, or a pharmaceutically acceptable salt thereof, wherein R³ and R⁴ taken together with the nitrogen to which they are attached form ~~piperazine, morpholine,~~ or pyrrolidine, ~~each~~ unsubstituted or substituted with C₁₋₄alkyl.

~~27.24.~~ The compound of claim ~~24 21~~, or a pharmaceutically acceptable salt thereof, wherein R³ and R⁴ taken together with the nitrogen to which they are attached form ~~piperazine or~~ morpholine, ~~each~~ unsubstituted or substituted with C₁₋₄alkyl.

~~28.25.~~ The compound of claim ~~24 21~~, or a pharmaceutically acceptable salt thereof, wherein R³ and R⁴ taken together with the nitrogen to which they are attached form piperazine, unsubstituted or substituted with C₁₋₄alkyl.

~~29.26.~~ The compound of claim ~~24 21~~, or a pharmaceutically acceptable salt thereof, wherein R³ and R⁴ taken together with the nitrogen to which they are attached form piperazine or 4-methylpiperazine.

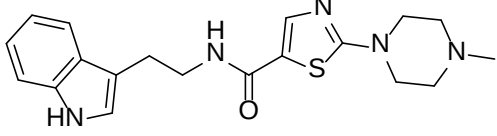
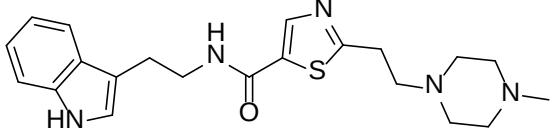
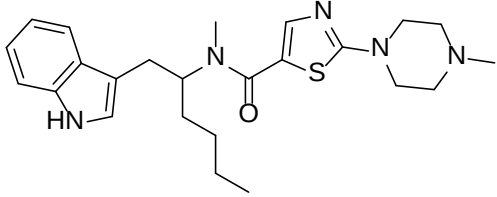
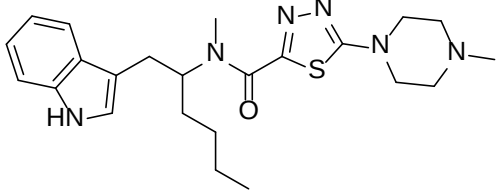
~~30.27.~~ The compound of any one of claims 1, ~~5-19, or 21-23~~ 3-16 and 18-20, or a pharmaceutically acceptable salt thereof, wherein Y is C₁₋₄alkylene, and R³ and Y taken together with the nitrogen to which R³ is attached form a monocyclic heterocycloalkyl ring, and R⁴ is H or C₁₋₄alkyl.

~~31.28.~~ The compound of claim ~~30 27~~, or a pharmaceutically acceptable salt thereof, wherein Y and R³ taken together with the nitrogen to which R³ is attached form pyrrolidine or piperidine.

~~32.29.~~ The compound of claim ~~30 27~~ or claim ~~31 28~~, or a pharmaceutically acceptable salt thereof, wherein R⁴ is H or methyl.

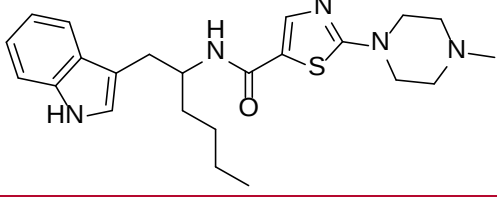
~~33.30.~~ The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is H, R² is C₁₋₄alkyl, A is thiazole, Y is absent or is ethylene, and R³ and R⁴ taken together with the nitrogen to which they are attached form N-methylpiperazine.

~~34.31.~~ A compound selected from the group consisting of:

	N-(2-(1H-Indol-3-yl)ethyl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide
	N-(2-(1H-Indol-3-yl)ethyl)-2-(2-(4-methylpiperazin-1-yl)ethyl)thiazole-5-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-N-methyl-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide
	N-(1-(1H-indol-3-yl)hexan-2-yl)-N-methyl-5-(4-methylpiperazin-1-yl)-1,3,4-thiadiazole-2-carboxamide

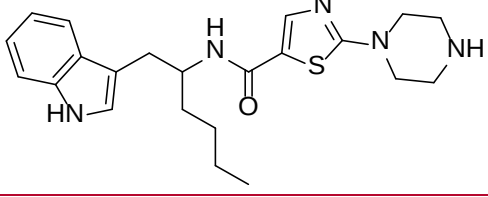
and pharmaceutically acceptable salts thereof.

32. The compound of claim 1, wherein the compound is

	<u>N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(4-methylpiperazin-1-yl)thiazole-5-carboxamide</u>
---	---

or a pharmaceutically acceptable salt thereof.

33. The compound of claim 1, wherein the compound is

	<u>N-(1-(1H-Indol-3-yl)hexan-2-yl)-2-(piperazin-1-yl)thiazole-5-carboxamide</u>
---	---

or a pharmaceutically acceptable salt thereof.

34. A pharmaceutical composition comprising (a) at least one compound or pharmaceutically acceptable salt thereof according to any one of claims 1 and 3-33, and (b) a pharmaceutically acceptable excipient.

35. The pharmaceutical composition of claim 34, wherein R² is substantially an “R” or substantially an “S” stereochemical configuration.

36. A pharmaceutical composition comprising (a) at least one compound or pharmaceutically acceptable salt thereof according to claim 2, and (b) a pharmaceutically acceptable excipient.

35-37. A compound or pharmaceutically acceptable salt according to any one of claims ~~1-2 or 5-34~~ 1-33 for use in the preparation of a medicament for the treatment of a disease or medical condition associated with protein aggregation.

36-38. Use of a compound or pharmaceutically acceptable salt thereof according to any one of claims ~~1-2 or 5-34~~ 1 to 33 in the preparation of a medicament for the treatment of a disease or medical condition associated with protein aggregation.

37-39. The ~~method of claim 4, the~~ compound or pharmaceutically acceptable salt of claim ~~35~~ 37, or the use of claim ~~36~~ 38, wherein the disease or medical condition associated with protein aggregation is Alzheimer’s disease, Parkinson’s disease, fronto-temporal dementia, dementia with Lewy bodies (Lewy body disease), Parkinson’s disease with dementia, multiple system atrophy, amyotrophic lateral sclerosis, Huntington’s disease, cancer, melanoma, or an inflammatory disease.

38-40. A method of interfering with the accumulation of protein or peptide aggregates in a cell, or preventing, slowing, reversing, or inhibiting protein or peptide aggregation in a cell, comprising contacting the cell with an effective amount of at least one compound or pharmaceutically acceptable salt according to any one of claims ~~1-2 or 5-34~~ 1-33, and/or with the pharmaceutical composition according to claim ~~3~~ 34, wherein the contacting is *in vitro*, or *ex vivo*, ~~or in vivo~~.