SUPPORTING INFORMATION

Table S1. Fixed-ratio combinations of ANTAG3 and linsitinib for median-effect analysis of dose equivalence.

Label	f	Treatment (nM) [ANTAG3]	Treatment (nM) [Linsitinib]	CI
ANTAG3 IC_{50}	1	3340	0	1
Lins IC_{50}	0	0	151	
1	0.75	2505	38	
2	0.5	1670	76	1
3	0.25	835	113	
4	0.75	1879	9	
5	0.5	1253	38	0.75
6	0.25	626	85	
7	0.75	1253	19	
8	0.5	835	38	0.5
9	0.25	418	57	
10	0.75	626	9	
11	0.5	418	19	0.25
12	0.25	209	28	

f = fixed-ratio constant; CI = combination index; Lins = linsitinib

Table S2. Fixed-ratio combinations of ANTAG3 and 1H7 for median-effect analysis of dose equivalence.

Label	f	Treatment (nM) [ANTAG3]	[1H7]	CI
ANTAG3 IC$_{50}$	1	3340	0	1
1H7 IC$_{50}$	0	0	14.3	
1	0.75	2505	3.6	
2	0.5	1670	7.2	1
3	0.25	835	10.7	
4	0.75	1879	2.7	
5	0.5	1253	5.4	0.75
6	0.25	626	8.0	
7	0.75	1253	1.8	
8	0.5	835	3.6	0.5
9	0.25	418	5.4	

f = fixed-ratio constant; CI = combination index

Table S3. Patient Characteristics

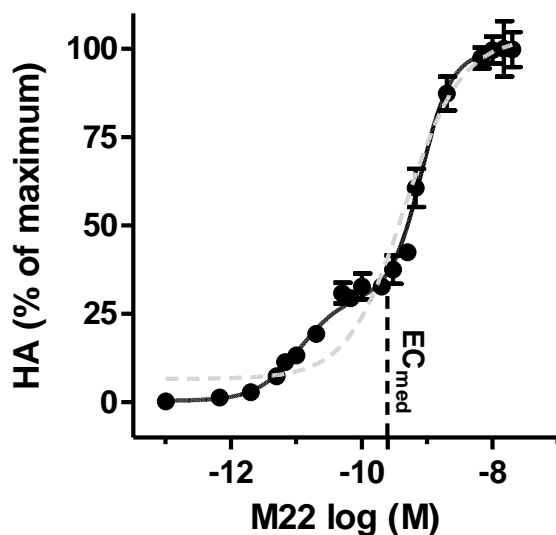| ID	Age	Sex	TSH (µIU/ml)	Free T4 (ng/dL)	TSI (%)	TRAb (IU/L)
GOB8	53	F	<0.01	1.9	330	13
GOB9	64	F	6.04	1	720	17
GOB10	49	F	<0.01	2.3	370	3.31
GOB11	27	F	<0.01	>5.0	600	9.96
GOB12	59	F	<0.01	2.2	500	>40
GOB13	53	M	0.23	1.5	770	>40
Normal Range	--	--	**0.27-4.2 µIU/ml**	**0.9-1.7 ng/dL**	**<140%**	**<1.7 IU/L**

Figure S1. M22 dose response in primary Graves' orbital fibroblasts.

Cultured GOF cells were stimulated with increasing concentrations of M22 for 5 days in order to generate a dose response curve. Total HA was measured in culture media by ELISA. Data represents mean ± SE from 3 different donor cell strains plotted as percent HA levels relative to maximal response. The curve fits to a biphasic model with an EC_{med} concentration estimated at 0.25±0.04 nM. The grey dotted line corresponds to a forced-fit monophasic model for comparison to the biphasic curve (solid black line). As previously described (Krieger et. al, 2015), fitting to the biphasic model was conducted by GraphPad Prism. The extra-sum-of-squares F test was conducted to discriminate between a monophasic and biphasic models and found the biphasic fit to be significantly better (P < 0.0001). Above data was generated from 3 different donor cell strains, which were not used in the previous publication.
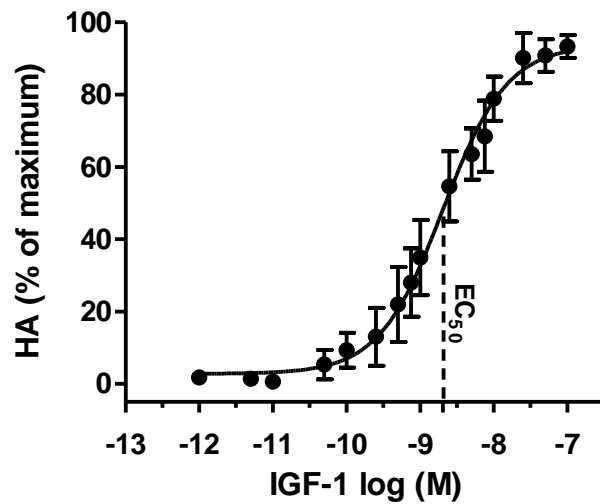
Figure S2. IGF-1 dose response in primary Graves' orbital fibroblasts.

Cultured GOF cells were stimulated with increasing concentrations of IGF-1 for 5 days in order to generate a dose response curve. Total HA was measured in culture media by ELISA. Data represents mean ± SE from 3 different donor cell strains plotted as percent HA levels relative to maximal response. The curve is monophasic with an EC_{50} concentration estimated at 2.05±1.59 nM. Please note EC_{max} values of IGF-1 in patient strains were comparatively ~70-80% of M22 EC_{max} for HA secretion (data not shown). This is consistent with previously published results (Krieger, Neumann, Place, Marcus-Samuels & Gershengorn, 2015).