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Bertinato et al.

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# (54) TRIAMIDE-SUBSTITUTED HETEROBICYCLIC COMPOUNDS

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(65) Prior Publication Data

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#### Related U.S. Application Data

- (60) Provisional application No. 60/301,644, filed on Jun. 28, 2001.
- (51) Int. Cl. A61K 31/405 (52) U.S. Cl. 514/415; 548/492
- (58) Field of Search ...... 548/492; 514/415

### (56) References Cited

### U.S. PATENT DOCUMENTS

4,022,900 A	<b>A</b> 5/1977	Mathison 424/258
4,397,855 A	A 8/1983	Sircar 424/250
5,416,009 A	<b>A</b> 5/1995	Lazzeri et al 435/69.3
5,712,279 A	A 1/1998	Biller et al 514/252
5,731,340 A	A 3/1998	Bras et al 514/415
5,741,804 A	4/1998	Keenan et al 514/394
5,919,795 A	<b>A</b> 7/1999	Chang et al 514/310
5,968,950 A	10/1999	Quallich et al 514/310
6,066,653 A	A 5/2000	Gregg et al 514/325
6,121,283 A	A 9/2000	Chang et al 514/307
6,197,798 H	3/2001	Fink et al 514/354
6,235,730 H	31 5/2001	Sato et al 514/211.11
6,281,228 H	31 8/2001	Tino 514/319
6,288,234 H	31 9/2001	Griffin 546/190
6,337,344 H	31 1/2002	Defossa et al 514/415
2002/0032238 A	<b>A</b> 1 3/2002	Priepke et al 514/616
		•

#### FOREIGN PATENT DOCUMENTS

DE	19945594	3/2001	C07D/295/04

EP	0643057	3/1995	C07D/401/04
EP	1080724	3/2001	A61K/31/195
EP	1181954	2/2002	A61P/3/06
EP	0584446	6/2002	C12N/15/12
WO	WO 0005201	2/2000	C07C/311/20
WO	WO 0105762	1/2001	C07D/211/00
WO	WO 0204403	1/2001	C07C/233/92
WO	WO 0121604	3/2001	C07D/295/14
WO	WO 0147898	7/2001	C07D/241/00
WO	WO 0147899	7/2001	C07D/241/04
WO	WO 0153260	7/2001	C07D/211/44
WO	WO 0177077	10/2001	C07D/213/38
WO	WO 0192241	12/2001	C07D/295/135
WO	WO 0196327	12/2001	C07D/401/12
WO	WO 0197810	12/2001	A61K/31/445
WO	WO 0242291	5/2002	C07D/401/06
WO	WO 0283658	10/2002	C07D/295/135

### OTHER PUBLICATIONS

Watterau, J.R., et al., *Science*, "Absence of Microsomal Triglycaride Transfer Protein in Individuals with Abetallpoproteinemia", vol. 258, (Nov. 6, 1992).

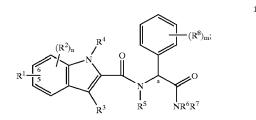
Watterau, J.R. et al., *Biochimica of Biophysica Acta*, "Localization of Intracellular Triacylglycerol and Cholesteryl Ester Transfer Activity In Rat Tissues", vol. 875 pp. 610–617 (1986).

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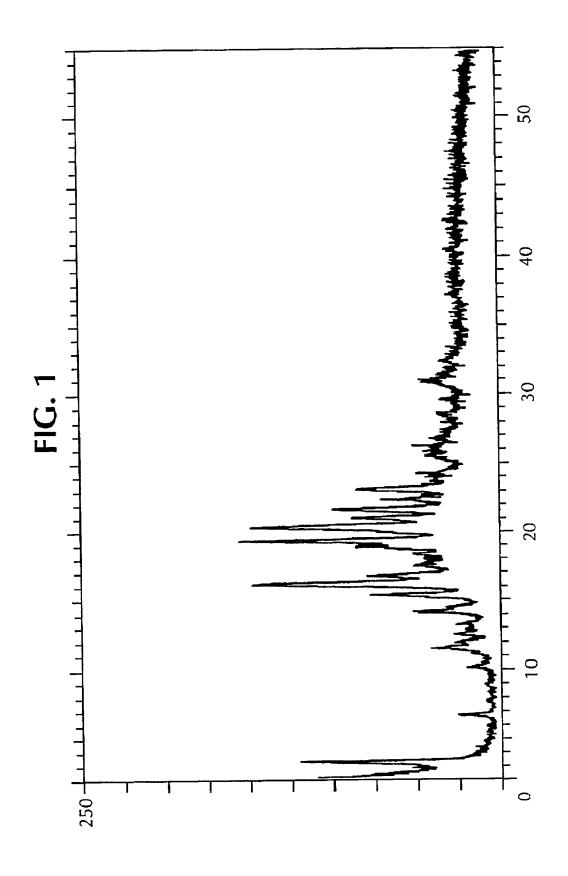
### (57) ABSTRACT

The invention relates to triamide MTP/ApoB inhibitors of the formula 1



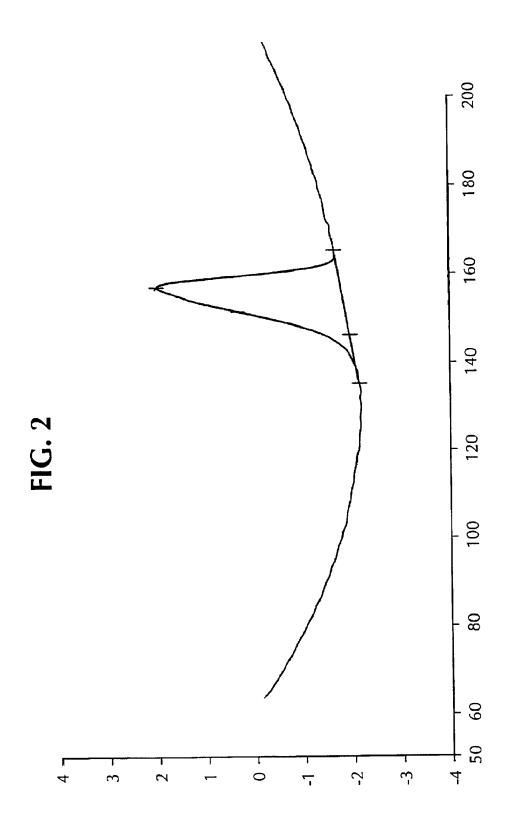
wherein  $R^1$ – $R^8$  are as defined in the specification, as well as pharmaceutical compositions and uses thereof, and processes for preparing the compounds. The compounds of the invention are useful for the treatment of obesity and lipid disorders.

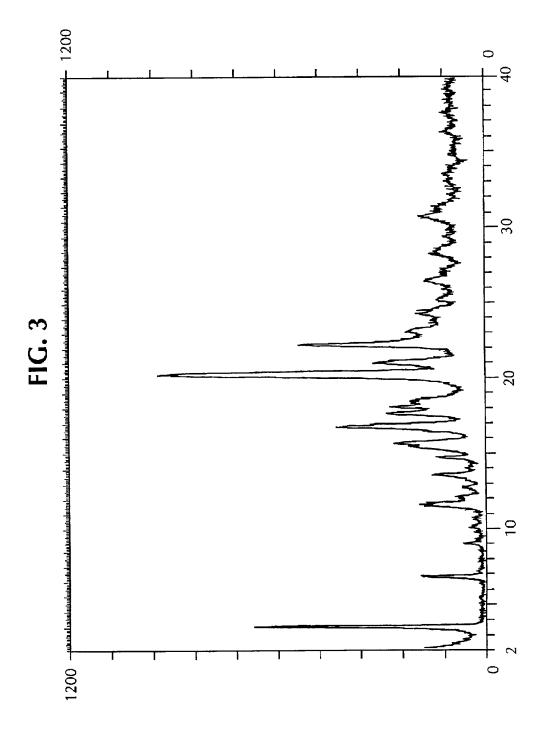
### 45 Claims, 6 Drawing Sheets



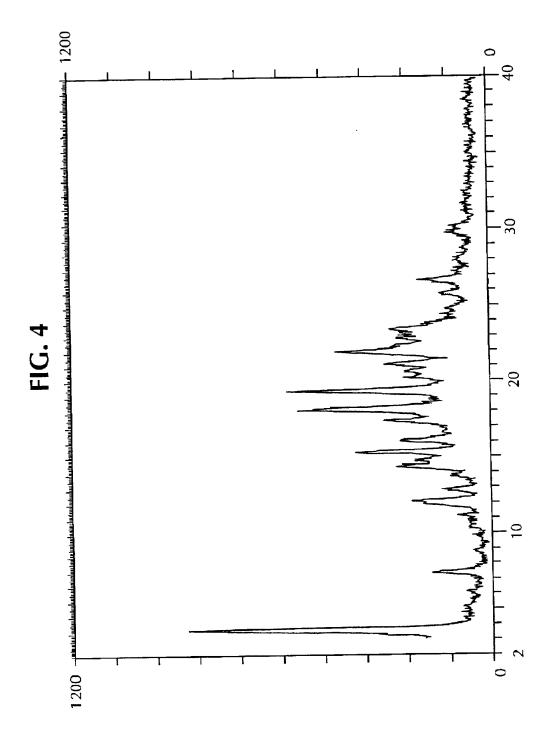


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