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# (12) United States Patent Lau et al.

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| (54) | ACYLATED GLP-1 COMPOUNDS   |      |   |  |  |
|------|----------------------------|------|---|--|--|
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| (52) | IIS CL      | ,         |

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### (56) References Cited

## U.S. PATENT DOCUMENTS

| 5,545,618 A      | 8/1996 | Buckley et al. |         |
|------------------|--------|----------------|---------|
| 6,268,343 B1*    | 7/2001 | Knudsen et al  | 514/4.8 |
| 6,528,486 B1*    | 3/2003 | Larsen et al   | 514/6.8 |
| 2007/0203058 A1* | 8/2007 | Lau et al.     |         |

#### FOREIGN PATENT DOCUMENTS

| EP | 05102171    | 3/2005  |  |
|----|-------------|---------|--|
| EP | 1704165     | 9/2006  |  |
| RU | 2006107600  | 10/2007 |  |
| WO | WO 91/11457 | 8/1991  |  |
| WO | WO 96/29342 | 9/1996  |  |
| WO | WO 9629342  | 9/1996  |  |
| WO | WO 98/08871 | 3/1998  |  |
| WO | WO9808871   | 3/1998  |  |
| WO | WO 99/43708 | 9/1999  |  |
| WO | WO9943708   | 9/1999  |  |
| WO | WO0034331   | 6/2000  |  |
| WO | WO 00/69911 | 11/2000 |  |
| WO | WO0069911   | 11/2000 |  |
|    |             |         |  |

| WO | WO 00/34331    | 6/2002  |
|----|----------------|---------|
| WO | WO 02/46227    | 6/2002  |
| WO | WO0246227      | 6/2002  |
| WO | WO 02/098446   | 12/2002 |
| WO | WO 03/040309   | 5/2003  |
| WO | WO 2004/065621 | 8/2004  |
| WO | WO 2004/099246 | 11/2004 |
| WO | WO 2005/014049 | 2/2005  |
| WO | WO2005014049   | 2/2005  |
| WO | WO 2005/027978 | 3/2005  |
| WO | WO2005027978   | 3/2005  |
| WO | WO 2006/097537 | 9/2006  |
|    |                |         |

#### OTHER PUBLICATIONS

Simonovsky et al. Poly(ether urethane)s incorporating long alkyl side-chains with terminal carboxy groups as fatty acid mimics: synthesis, structural characterization and protein adsorption. Journal of Biomaterials Science, Polymer Edition, 2005, vol. 16, No. 12, pp. 1463-1483.\*

Green, Brian D., Biological Chemistry (2004), vol. 385, No. 2, pp. 169-177.

Knudsen, L.B. et al., Journal of Medicinal Chemistry, vol. 43, pp. 1664-1669 (2000).

Knudsen, L.B. et al., Journal of Medicinal Chemistry, vol. 47, pp. 4128-4134 (2004).

Deacon, C.F. et al., Diabetologia, vol. 41, pp. 271-278 (1998).

Greenwald RB, "Peg Drugs: An Overview," Journal of Controlled Release, 2001, vol. 74, p. 159-171.

Ji et al., "Stearyl Poly(Ethylene Oxide) Grafted Surfaces for Preferential Adsorption of Albmnin," Biomaterials, 2001, vol. 22, p. 3015-3023.

Kurtzhals, P, et al., "Albumin Binding of Insulins Acylated With Fatty Acids: Characterization of the Ligand-Protein Interaction and Correlation Between Binding Affinity and Timing of the Insulin Effect in Vivo," Biochem J, 1995, vol. 312, p. 725-731.

Simonovsky et al., "Poly(Etherurethane)s Incorporating Long Alkyl Side-Chains With Terminal Carboxyl Groups as Fatty Acid Mimics: Synthesis, Structural Characterization and Protein Adsorption," J Biomat Sei Polymer EDN, 2005, vol. 16, p. 1463-1483.

Soltero et al., "The Oral Delivery of Protein and Peptide Drugs," Innovations in Pharmaceutical Technology, 2001, vol. 1, No. 9, p. 106-110.

Still JG, "Development of Oral Insulin: Progress and Curent Status," Diabetes/Metab Res Rev, 2002, vol. 18, Suppl 1, p. S29-S37.

Veronese FM, "Peptide and Protein Pegylation: A Review of Problems and Solutions," Biomaterials, 2001, vol. 22, p. 405-417. Watanabe et al., "Structure-Activity Relationships of Glucagon-Like Peptide-1 (7-36) Amide: Insulinotropic Activities in Perfused Rat Pancreases, and Receptor Binding and Cyclic Amp Production in RINm5F Cells," Journal of Endocrinology, 1994, vol. 140, p. 45-52.

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## (57) ABSTRACT

Protracted GLP-1 compounds and therapeutic uses thereof.

6 Claims, No Drawings

<sup>\*</sup> cited by examiner