

Title (en)  
BIOCONJUGATION IN VIVO TO PULMONARY OR BLOOD COMPONENTS

Title (de)  
IN VIVO BIOKONJUGIERUNG AN PULMONÄREN ODER BLUTKOMPONENTEN

Title (fr)  
DIFFUSION PULMONAIRE PERMETTANT LA BIOCONJUGAISON

Publication  
**EP 1235618 A2 20020904 (EN)**

Application  
**EP 00962766 A 20000907**

Priority  
• IB 0001429 W 20000907  
• US 15268199 P 19990907

Abstract (en)  
[origin: WO0117568A2] Methods of and compositions for pulmonary delivery of therapeutic agents which are capable of forming covalent bonds with a site of interest or which have formed a covalent bond with a pulmonary solution protein are disclosed. Therapeutic agents useful in the invention include wound healing agents, antibiotics, anti-inflammatories, anti-oxidants, anti-proliferatives, immunosuppressants, anti-infective and anti-cancer agents.  
[origin: WO0117568A2] In order to meet these needs, the present invention is directed to therapeutic and diagnostic agents capable of forming covalent bonds to blood and pulmonary fluid proteins or other components ex vivo or in vivo. The therapeutic agents of this invention have a long duration of action for the management of disease. The invention relates to ex vivo and in vivo bioconjugation of therapeutic agents to protein (e.g. albumin), as well as an intrapulmonary in vivo bioconjugation of therapeutic agents to endogenous pulmonary fluid proteins or other components to dramatically increase the half life of the therapeutic agents and avoid the need for parenteral administration. This invention is further directed to the use of reactive chemistries including: N-hydroxy sulfosuccinimide, maleimide-benzoyl-succinimide, gamma-maleimido-butyryloxy succinimide ester, maleimidopropionic acid, isocyanate, thiolester, thionocarboxylic acid ester, imino ester, and carbodiimide anhydride. Maleimidopropionic acid is the preferred reactive chemistry, but the invention also contemplates the selection of the above and like reactive chemistries as an electrophilic moiety for bioconjugations with albumin or other proteins. Modified therapeutic agents mentioned are the anti-histamine drug loratidine or cetirizine, a hypothyroid drug, the anti-angina drug tirofiban, the anti-hypertensive drug enalapril, the anti-arrhythmic drug capobenic acid, the antidepressant drug fluoxetine, the bronchodilation drug the obromineacetamine, the antiinflammatory drug loxoprofen, the anti-thyroid deficiency drug thyroxin, and 4-anilino-1-(2-phenethyl)piperidine.

IPC 1-7  
**A61P 35/00**; **A61K 47/48**; **A61K 31/495**; **A61K 31/498**; **A61K 31/401**; **A61K 31/192**; **A61K 31/522**; **A61K 31/138**; **A61K 31/198**; **A61K 31/4468**; **A61P 11/06**; **A61P 37/08**; **A61P 5/16**; **A61P 9/10**; **A61P 9/12**; **A61P 9/06**; **A61P 25/24**; **A61P 11/08**; **A61P 29/00**; **A61P 5/14**

IPC 8 full level  
**C07D 473/10** (2006.01); **A61K 9/00** (2006.01); **A61K 9/12** (2006.01); **A61K 9/14** (2006.01); **A61K 31/138** (2006.01); **A61K 31/192** (2006.01); **A61K 31/401** (2006.01); **A61K 31/4015** (2006.01); **A61K 31/4025** (2006.01); **A61K 31/407** (2006.01); **A61K 31/437** (2006.01); **A61K 31/454** (2006.01); **A61K 31/4545** (2006.01); **A61K 31/496** (2006.01); **A61K 31/519** (2006.01); **A61K 31/522** (2006.01); **A61K 38/00** (2006.01); **A61K 38/22** (2006.01); **A61K 38/55** (2006.01); **A61K 47/42** (2006.01); **A61K 47/48** (2006.01); **A61P 3/10** (2006.01); **A61P 5/10** (2006.01); **A61P 5/14** (2006.01); **A61P 5/16** (2006.01); **A61P 5/38** (2006.01); **A61P 9/00** (2006.01); **A61P 9/06** (2006.01); **A61P 9/10** (2006.01); **A61P 9/12** (2006.01); **A61P 11/00** (2006.01); **A61P 11/06** (2006.01); **A61P 11/08** (2006.01); **A61P 25/00** (2006.01); **A61P 25/04** (2006.01); **A61P 25/24** (2006.01); **A61P 29/00** (2006.01); **A61P 31/00** (2006.01); **A61P 31/12** (2006.01); **A61P 31/18** (2006.01); **A61P 35/00** (2006.01); **A61P 37/06** (2006.01); **A61P 37/08** (2006.01); **A61P 41/00** (2006.01); **A61P 43/00** (2006.01); **C07D 207/452** (2006.01); **C07D 401/12** (2006.01); **C07D 401/14** (2006.01); **C07D 405/12** (2006.01); **C07D 475/08** (2006.01); **C07D 487/14** (2006.01); **C07D 519/04** (2006.01)

CPC (source: EP)  
**A61K 9/0075** (2013.01); **A61K 31/704** (2013.01); **A61K 47/643** (2017.07); **A61P 3/10** (2017.12); **A61P 5/10** (2017.12); **A61P 5/14** (2017.12); **A61P 5/16** (2017.12); **A61P 5/38** (2017.12); **A61P 9/00** (2017.12); **A61P 9/06** (2017.12); **A61P 9/10** (2017.12); **A61P 9/12** (2017.12); **A61P 11/00** (2017.12); **A61P 11/06** (2017.12); **A61P 11/08** (2017.12); **A61P 25/00** (2017.12); **A61P 25/04** (2017.12); **A61P 25/24** (2017.12); **A61P 29/00** (2017.12); **A61P 31/00** (2017.12); **A61P 31/12** (2017.12); **A61P 31/18** (2017.12); **A61P 35/00** (2017.12); **A61P 37/06** (2017.12); **A61P 37/08** (2017.12); **A61P 41/00** (2017.12); **A61P 43/00** (2017.12)

Citation (search report)  
See references of WO 0117568A2

Designated contracting state (EPC)  
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

DOCDB simple family (publication)  
**WO 0117568 A2 20010315**; **WO 0117568 A3 20020711**; AU 2005203768 A1 20050915; AU 7440400 A 20010410; AU 7440600 A 20010410; AU 781380 B2 20050519; CA 2383794 A1 20010315; CA 2383798 A1 20010315; EP 1212120 A2 20020612; EP 1235618 A2 20020904; JP 2003508501 A 20030304; JP 2003508502 A 20030304; WO 0117614 A2 20010315; WO 0117614 A3 20020228

DOCDB simple family (application)  
**IB 0001429 W 20000907**; AU 2005203768 A 20050822; AU 7440400 A 20000907; AU 7440600 A 20000907; CA 2383794 A 20000907; CA 2383798 A 20000907; EP 00962764 A 20000907; EP 00962766 A 20000907; IB 0001427 W 20000907; JP 2001521356 A 20000907; JP 2001521398 A 20000907