A composition comprises a nucleic acid comprising an oligo anti-sense to a target such as polypeptide(s) associated with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixtures. Various formulations contain a requisite carrier, and optionally other additives and biologically active agents. The agent of the invention may be prepared by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) associated with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more anti-sense oligonucleotide(s) to the mRNA segments which are free of adenose (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepared by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the anti-sense oligonucleotides with a Universal base@. The agent, composition and formulations are used for prophylactic, preventive and therapeutic treatment of ailments associated with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasosconstriction, inflammation, allergies, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, antibody therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs.
# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**
IPC(7) : C07H 21/04; A61K 48/00; C12N 15/12
US CL : 536/24.5; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC.

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched.

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

- Medline, Biosis, US Patent database, Derwent WPI
- search terms: adenosine A1 receptor, antisense

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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<td>US 5,932,557 A (MUSTAFA et al.) 03 August 1999, column 6, line 14.</td>
<td>1, 15-17, 24-28</td>
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**Further documents are listed in the continuation of Box C.**

**See patent family annex.**

**Date of the actual completion of the international search**
29 JANUARY 2000

**Date of mailing of the international search report**
10 FEB 2000

**Name and mailing address of the ISA/US**
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

**Authorized officer**
JOHN S. BRUSCA

**Telephone No.** (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1992)
INTERNATIONAL SEARCH REPORT

Box I  Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. ☑ Claims Nos.: 2-14, 18-23, 29-64, 74-77, 80, 82-85, 87-99, 102-112, 121-124, 127-130, 132-148 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

   Please See Extra Sheet.

3. ☐ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II  Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant’s protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1))(July 1992)★
BOX I. OBSERVATIONS WHERE CLAIMS WERE FOUND UNSEARCHABLE

2. Where no meaningful search could be carried out, specifically:

Claim 18 was not searched because the claim is drawn to nucleic acid sequences and the computer readable form was defective. The other unsearched claims were not searched because they are drawn to a multitude of embodiments that are not related to the exemplified invention. Claims drawn to the exemplified invention have been searched.