data, NCI-sponsored clinical trials to examine the potential of arsenic trioxide for the treatment of solid tumours are under way or in the final planning stages.

4. Summary of the ~~Invention~~Disclosure

The present ~~invention~~disclosure relates to a pharmaceutical composition intended for the treatment of urogenital diseases and bone metastasis and to a method of treating such diseases.

Accordingly, the present ~~invention~~disclosure provides a pharmaceutical composition intended for the treatment of urogenital diseases and bone metastasis in a human, wherein said pharmaceutical composition contains an effective amount of arsenous acid alkaline or earth alkaline metal salt and/or a pharmaceutically acceptable adjuvant.

According to the present ~~invention~~disclosure, said alkaline arsenous acid metal salt is sodium meta-arsenite (AsO_2Na) or potassium meta-arsenite (AsO_2K).

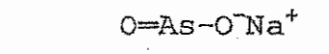
The effective amount of arsenous acid alkaline or earth alkaline metal salt is 0.0001-1500 mg/kg, preferably 1-1000 mg/kg, more preferably 1-150 mg/kg, and most preferably 50-100 mg/kg of body weight/day.

Said pharmaceutical composition preferably occurs in an oral administration form, wherein said oral administration form is e.g. a tablet, capsule, powder and/or solution with

a pharmaceutically acceptable carrier, diluent or excipient.

Said urogenital disease comprises essentially cancer of the prostate, bladder, kidney and testis.

According to the ~~invention~~disclosure, a chemotherapeutic product comprises of arsenous acid sodium salt having the formula (I):



Furthermore, the ~~invention~~disclosure includes pharmaceutical compositions comprising such products together with a pharmaceutically acceptable carrier or diluent. Suitable carriers and diluents are well known, as are the principles of formulation of compositions in unit dosage form and for oral administration.

In a further aspect, the ~~invention~~disclosure includes a method for the treatment of cancer in an animal or human body, the method comprising the simultaneous, separate or sequential administration to the said body of arsenous acid sodium salt.

In a first aspect, there is provided the use of sodium meta arsenite and one or more pharmaceutically acceptable: adjuvants; excipients; carriers; buffers; and diluents, for the manufacture of a medicament for the treatment of leukemia or lymphoma in a patient, said medicament comprising an oral dosage form of sodium meta arsenite in a therapeutically effective amount in the range of from 2.5mg to 7g/day.

In a second aspect, there is provided a kit for inhibiting abnormal cell growth comprising of arsenous acid sodium salt and/or synthetic analogues, modifications and pharmacologically active fragments thereof.

The Inventor has explored the potency of three arsenic compounds of different valence and methylation in panels of human tumour cell lines in vitro, arsenous acid sodium salt (As^{3+}), dimethylarsinic acid (As^{5+}) and arsenic acid (As^{5+}). Surprisingly arsenous acid sodium salt was the most potent and showed anti-tumour activity in a human tumour model in

vivo, reason to develop arsenous acid sodium salt further as a novel arsenic compound. Arsenous acid sodium salt surprisingly was more potent in vitro and showed differential activity in leukaemia, melanoma and mammary cancer lines than As_2O_3. Arsenous acid sodium salt is surprisingly capable of shortening telomeres of human cancer cells, inducing cellular senescence and chromosomal abnormalities, but does not directly inhibit the telomerase activity. The effects indicate that arsenous acid sodium salt is a telomere inhibitor. Arsenous acid sodium salt was rapidly absorbed after both i.v. and p.o. administration and remained in the plasma for prolonged periods. Surprisingly the bioavailability of oral arsenous acid sodium salt was approximately 100%. Animal toxicity studies showed that the main target organs were bone marrow and lymphoid organs. Thus arsenous acid sodium salt can be administered orally. It might be used in long-term treatment of cancer patients with solid tumours or leukaemia at dose levels below the maximum tolerated dose (MTD), alone or in combination with another treatment modality, maintaining a good quality of life.

This compound ($NaAsO_2$) of the present ~~invention~~disclosure has been developed as novel anti-cancer agent. The compound possesses good cytotoxic activity in a panel of 43 human tumour cell lines in vitro with an IC50 value of 0.6 µM. Pronounced selectivity was observed in tumour cell lines derived from leukaemia, mammary cancer and melanoma. In a head-to-head comparison arsenous acid sodium salt was surprisingly at least 15-fold more potent than the clinically used agent arsenic trioxide and had also a

Surprisingly arsenous acid sodium salt, the compound of ~~inventiondisclosure~~, has great therapeutic and safety advantages in comparison to arsenic trioxide. Arsenic trioxide As_2O_3 has been shown to prolong the QT and QT interval corrected for rate (QT_c), which may predispose the patient to potentially fatal aytipical ventricular tachycardia and produce complete atrioventricular block.

Further more, adverse events occurring in 10% or more of patients treated with arsenic trioxide include fatigue, fever, oedema, chest pain, rigors, reactions at the injection site (ie pain, erythema, oedema), weakness, weight gain, nausea, anorexia, decreased appetite, diarrhoea or loose stools, vomiting, abdominal pain, dyspepsia, sore throat, constipation, hypokalemia, hypomagnesemia, increases in serum AST (SGOT) and/or ALT (SGPT), hyperkalemia, hypocalcemia, headache, insomnia, paresthesia, dizziness, tremor, cough, dyspnea, epistaxis, hypoxia, pleural effusion, postnasal drip, wheezing, decreased breath sounds, crepitations, rales, dermatitis, pruritus, ecchymosis, dry skin, erythema, sweating, tachycardia, ECG abnormalities, sinusitis, herpes simplex, upper respiratory infection, arthralgia, myalgia, bone pain, back pain, neck pain, limb pain, leukocytosis, anaemia, thrombocytopenia, neutopenia (may be febrile), hypotension, hypertension, flushing, pallor, anxiety, depression, ocular irritation, blurred vision and vaginal haemorrhage.

Surprisingly none of these adverse events have been observed using the oral arsenous acid sodium salt, which is the compound of the present ~~inventiondisclosure~~.