
ATON
PHARMA

About Aton Pharma, Inc.

- Previously a wholly-owned subsidiary of Merck & Co. Inc.
- Purchased from Merck in October of 2006 by Princeton Pharma Holdings, LLC,
  - Aton is now a wholly-owned subsidiary of Princeton Pharma Holdings
  - Financing provided by Cerberus Capital Management, LLC, one of the world's largest private equity firms
- Aton owns worldwide rights to eight medically significant products
- Product sales and donations in over 30 countries
- A leader in the treatment of rare conditions
- Company headquartered in Princeton, New Jersey, U.S.A.
- Management with global pharmaceutical experience

ATON PHARMA

Our Products

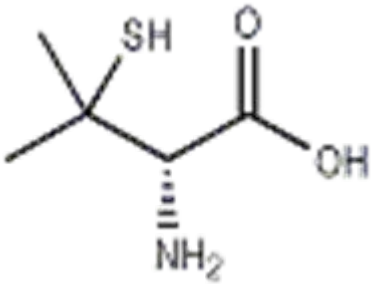
Cardiovascular	
AquaMephyton®	Coagulation disorders
Mephyton®	Coagulation disorders
Edecrin®	Edema, sulfa allergy
Sodium Edecrin®	Edema sulfa allergy
Metabolic Disease	
Cuprimine®	Wilson's Disease
Syprine®	Wilson's Disease
Demser®	Pheochromocytoma
Ophthalmology	
Lacrisert®	Dry Eye Syndrome

ATON PHARMA

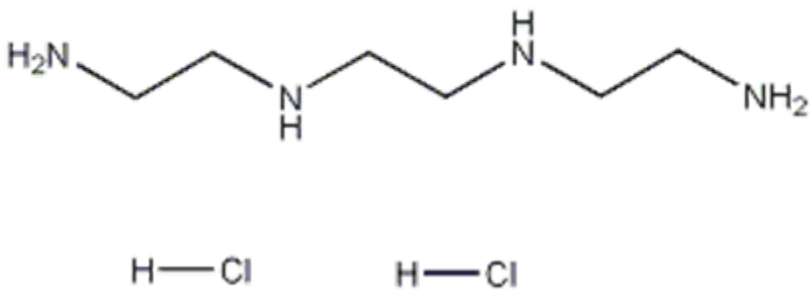
Aton Chelators

Remove excess of copper from the body in Wilson Disease

- Cuprimine® brand penicillamine, FDA approved 1963
  - Orally active, approved for Wilson Disease, rheumatoid arthritis, cystinuria, and in some countries, lead poisoning
  - Available as 250 mg capsules



- Syprine® brand trientine, FDA approved 1985
  - Orally active, approved for Wilson Disease
  - Available as 250 mg capsules



ATON PHARMA

Current Situation

- CUPRIMINE® is listed on the Radiation Event Medical Management website (www.remm.nlm.gov) as a countermeasure for the following isotopes
  - Copper, Iron, Mercury, Lead, Gold and possibly other heavy metals
- Because of this listing Aton is required to provide an inventory and scale-up report for CUPRIMINE® to the FDA's Drug Shortage Division every six months
- CUPRIMINE® is stockpiled in limited quantities by Los Angeles County Emergency Medical Services Agency[1]
- The clinical utility of CUPRMINE® for Wilson's Disease and rheumatoid arthritis is decreasing
  - Due to emergence of Zinc Acetate for long term use and preferential use of SYPRINE® – Aton's other chelator
  - Long term commercial viability of CUPRMINE® is uncertain
- SYPRINE® can potentially be used as a countermeasure for additional isotopes beyond those covered by CUPRIMINE®
- CDC is currently stockpiling two other chelating agents
  - DTPA (for Pu, Am, Cm) and Prussian Blue (for Cs)

[1]Marcus, CS. Administration of decorporation drugs to treat internal radionuclide contamination: medical emergency response to radiologic incidents. RSO Magazine, 2004;9(5):9-15.

ATON PHARMA

Recent News Reinforces the Needs

Improve Prevention and Prepare Response

The New York Times nytimes.com

July 12, 2007

A Nuclear Ruse Uncovers Holes in U.S. Security

By ERIC LIPTON

WASHINGTON, July 11 — Undercover Congressional investigators set up a bogus company and obtained a license from the Nuclear Regulatory Commission in March that would have allowed them to buy the radioactive materials needed for a so-called dirty bomb…. The machines include americium-241 and cesium-137, radioactive substances commonly used in industrial equipment.

CNN.com

Americans believed poisoned in Moscow

POSTED: 9:51 a.m. EST, March 7, 2007

MOSCOW, Russia (CNN) -- Two American women have been released from a Moscow clinic after they were hospitalized with possible thallium poisoning, a hospital official said…. The U.S. Embassy confirmed earlier on Wednesday that the women had possibly been poisoned from thallium, a radioactive element….Thallium is a colorless, tasteless substance that can be fatal in doses of as little as one gram and has the reputation as a poison of choice for assassins. It was used by Saddam Hussein to kill several of his Iraqi opponents, AP said.

AP Associated Press

Ex-KGB agent accused in Litvinenko death

By TARIQ PANJA, Associated Press Writer*1 hour, 15 minutes ago*

Prosecutors accused a former KGB agent Tuesday of murder in the radioactive poisoning of fellow ex-operative Alexander Litvinenko and sought his extradition from Russia. The case is sure to challenge already-tense relations between London and Moscow. Andrei Lugovoi had met with Litvinenko at a London hotel hours before the former agent turned Kremlin critic fell ill with polonium-210 poisoning.

ATON PHARMA

Recent News Reinforces the Needs *(cont.)*

Improve Prevention and Prepare Response

The New York Times
nytimes.com

August 1, 2007
Op-Ed Contributors

Seize the Cesium

By PETER D. ZIMMERMAN, JAMES M. ACTON and M. BROOKE ROGERS

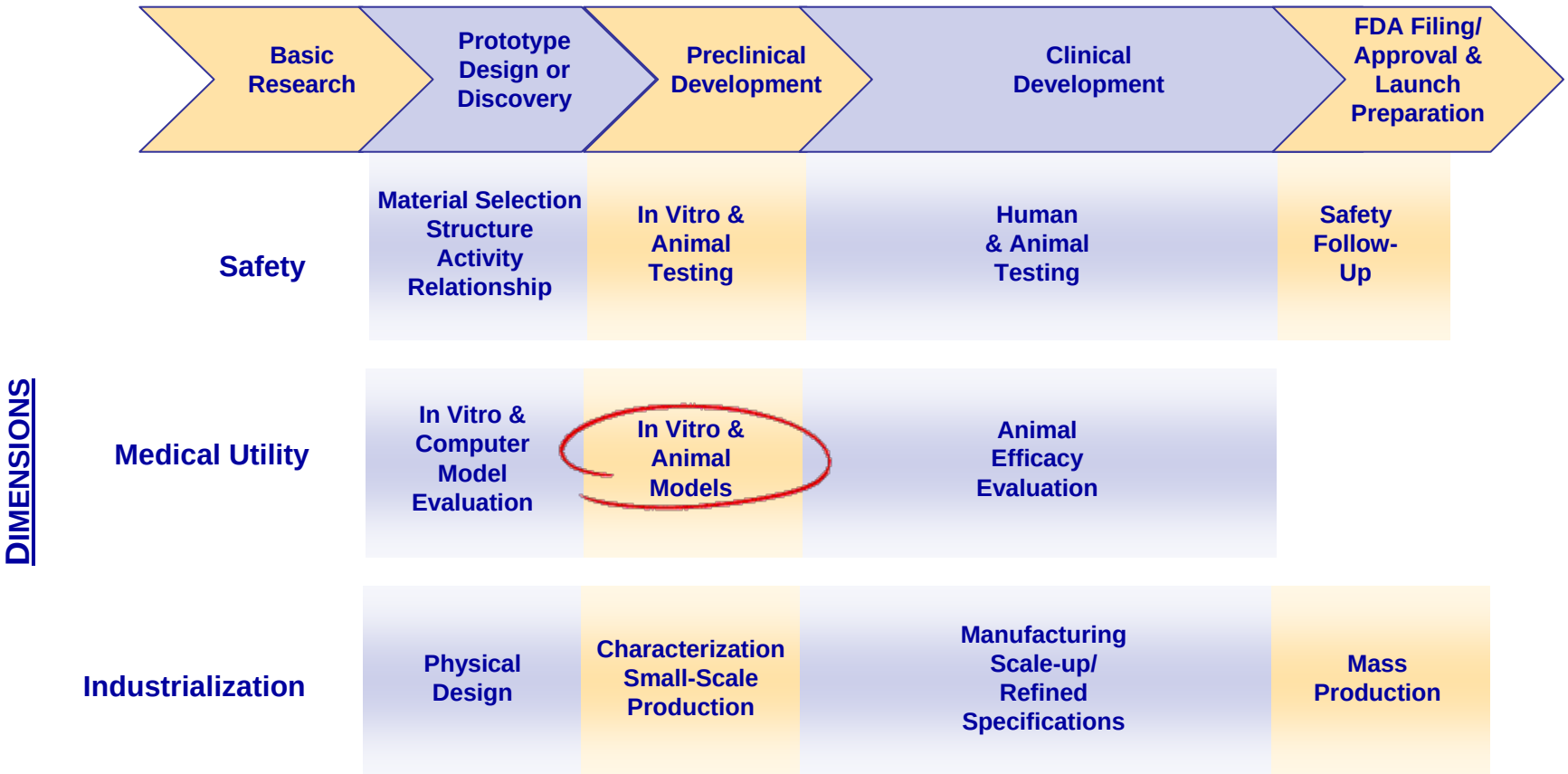
London

THE death of Alexander Litvinenko, the former K.G.B. officer who drank polonium-210 in a cup of tea, underscored the damage that radiological terrorists could do. The most familiar possible situations involve the detonation of a dirty bomb, a modest amount of high explosive mated to a container of radioactive material. **But radioactive material inside the human body is far more dangerous than a dirty bomb.**

Most analysts believe that about 10 people would die from radiation poisoning after a dirty bomb attack. Others believe that the only people likely to receive a lethal dose of radiation from a dirty bomb would already be dead from the blast. **A perfectly feasible terrorist attack using the ingestion, inhalation or immersion of radioactive material, on the other hand, would be almost certain to kill hundreds. We call attacks of these kinds I-cubed attacks (for ingestion, inhalation and immersion). Such attacks can be sneaky, unaccompanied by a flash and bang.**

ATON PHARMA

Technology Readiness Levels



TRL	1	2	3	4	5	6	7	8	9	10	11/12/13

Source:
Matthew Lawlor, Office of Public Health Emergency Medical Countermeasures, HHS.
Adapted from Innovation/Stagnation (FDA, March 2004)

ATON PHARMA

Binding of Metal Ions to Aton Chelators

Stability Constants (-logK_d)

Metal Ion	Trientine (Syprine®)	Penicillamine (Cuprimine®)
Copper	**20.05 (Cu^{+2})**	**18.18 (Cu^{+1})**
Palladium (Pd^{+2})	39.4	
Mercury (Hg^{+2})	24.5	16.3
Bismuth (Bi^{+3})	21.9	
Nickel (Ni^{+2})	13.8	10.70
Zinc (Zn^{+2})	12	9.71
Cadmium (Cd^{+2})	10.6	11.55
Cobalt (Co^{+2})	10.9	8.98
Lead (Pb^{+2})	10.4	12.3
Chromium (Cr^{+2})	7.9	
Iron (Fe^{+2})	7.76	
Silver (Ag^{+1})	7.5	12.4
Manganese (Mn^{+2})	4.90	
Indium (In^{+3})**		15.33
Thallium (Tl^{+1})*		3.58

Sources: Critically Selected Stability Constants of Metal Complexes. NIST Std. Ref. Database 46, December 1997.
Critical Stability Constants. A.E. Martell & R.M. Smith, Vols. 2, 5, 6 (NY: Plenum, 1974, 1982, 1989)
Handbook of Metal Ligand Heats, 3rd ed. J.J. Christensen & R.M.Izatt (NY: Marcel Dekker, Inc., 1983)
25°C, 0.1 M ionic strength, unless otherwise noted. *37°C **20°C

ATON PHARMA

Aton Chelators Bind Strongly to Certain Metals

Trientine (Syprine®)	Penicillamine (Cuprimine®)
Very Strongly:	Very Strongly:
Copper	Copper
Mercury	Mercury
Nickel	Indium
Bismuth	
Palladium	
Less Strongly:	Less Strongly:
Zinc	Zinc
Cadmium	Cadmium
Lead	Lead
Cobalt	Cobalt, Nickel, Silver

Sources:
Critically Selected Stability Constants of Metal Complexes. NIST Std. Ref. Database 46, December 1997.
Critical Stability Constants. A.E. Martell & R.M. Smith, Vols. 2, 5, 6 (NY: Plenum, 1974, 1982, 1989)
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ATON PHARMA

Evidence of Efficacy for Penicillamine

Decorporation of Cobalt

- Lé, Nature 204, 696-7 (1964): comparison of chelators to promote excretion of ^{60}Co in rats:
  - Single i.p. injection following i.v. ^{60}Co, equimolar doses
  - Penicillamine > DTPA > EDTA
  - **Penicillamine orally is at least as effective as injected**

Residual ^{60}Co dose in target organ (% of injected at 48h)†

Treatment	Kidney	Liver	Muscle	Bone
Control	0.84	4.86	2.14	0.58
EDTA	0.96	2.60	1.45	0.37
DTPA	1.20	1.83	0.88	0.11
Penicillamine‡ (injected)	0.20	0.86	0.73	0.26
Penicillamine‡ (oral)	0.15	0.58	0.59	0.14

†Mean of 5-6 rats/group; SD omitted for presentation purposes, but highly significant differences

‡ Referred to as DMCy (D-β,β'-dimethylcysteine)

ATON PHARMA

Evidence of Efficacy for Penicillamine (cont.)

Decorporation of Cobalt

with ^{60}Co is obvious. However, the highest significance must be attributed to D-dimethylcysteine (commonly known as penicillamine). Its high efficacy compares favourably with BADS and BATE. Our experimental data show that it can be administered orally without loss of effectiveness. Finally, its low toxicity must be stressed. More detailed studies on the effectiveness of

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Evidence of Efficacy for Penicillamine (cont.)

Decorporation of Cobalt

- Bibow et al., Acta Pharmacol. Toxicol. (Copenhagen) 59, suppl. 7, 374-7 (1986): +/- penicillamine in 2 women treated for RA
  - Measurement of metabolic balance of trace elements on controlled diet
  - Penicillamine (500 or 750 mg/d) promoted excretion of Zn and Co in urine
  - Cobalt excretion increased 5x

ATON PHARMA

“Dirty Bomb” Candidate Isotopes

- Radionuclides predicted to be of interest to terrorist, based on accessibility and maximizing impact include:

Americium-241

Californium-252

Cesium-137

Cobalt-60

Curium-243, -244

Hydrogen-3 (tritium)

Iodine-125, -131

Iridium-192

Palladium-103

Phosphorus-32

Plutonium-238, -239

Polonium-210

Radium-226

Strontium-90 (Sr-90/Y-90)

Uranium-234, -235

Sources:
Marcus, C.S. et al. (2006) Medical Management of Internally Radiocontaminated Patients, funded by grant EMW 2004-GR-0793 from Department of Homeland Security Metropolitan Medical Response System, available at County of Los Angeles Health Services website, http://ladhs.org/ems/disaster/mmrsmanual.pdf and REMM website, http://remm.nlm.gov/DMAT-Adm_Decorp_Drugs_Int_Rad_Contam_12-01-0311.pdf.
US DHHS Radiation Event Medical Management (REMM) website, http://remm.nlm.gov/rdd.htm#isotopes.

ATON PHARMA

CUPRIMINE

Dirty Bomb

PERIODIC CHART OF THE ELEMENTS

Known Very Strongly Binding

Known Less Strongly Binding

IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIII		IB	IIB	IIIA	IVA	VA	VIA	VIIA	INERT GASES
1 H 1.00797															1 H 1.00797	2 He 4.0026
3 Li 6.939	4 Be 9.0122										5 B 10.811	6 C 12.0112	7 N 14.0067	8 O 15.9994	9 F 18.9984	10 Ne 20.183
11 Na 22.9898	12 Mg 24.312										13 Al 26.9815	14 Si 28.086	15 P 30.9738	16 S 32.064	17 Cl 35.453	18 Ar 39.948
19 K 39.102	20 Ca 40.08	21 Sc 44.956	22 Ti 47.90	23 V 50.942	24 Cr 51.996	25 Mn 54.9380	26 Fe 55.847	27 Co 58.9332	28 Ni 58.71	29 Cu 63.54	30 Zn 65.37	31 Ga 69.72	32 Ge 72.59	33 As 74.9216	34 Se 78.96	35 Br 79.909	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.905	40 Zr 91.22	41 Nb 92.906	42 Mo 95.94	43 Tc (99)	44 Ru 101.07	45 Rh 102.905	46 Pd 106.4	47 Ag 107.870	48 Cd 112.40	49 In 114.82	50 Sn 118.69	51 Sb 121.75	52 Te 127.60	53 I 126.904	54 Xe 131.30
55 Cs 132.905	56 Ba 137.34	*57 La 138.91	72 Hf 178.49	73 Ta 180.948	74 W 183.85	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.09	79 Au 196.967	80 Hg 200.59	81 Tl 204.37	82 Pb 207.19	83 Bi 208.980	84 Po (210)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	‡89 Ac (227)	104 Rf (261)	105 Db (262)	106 Sg (266)	107 Bh (262)	108 Hs (265)	109 Mt (266)	110 ? (271)	111 ? (272)	112 ? (277)						

Numbers in parenthesis are mass numbers of most stable or most common isotope.

Atomic weights corrected to conform to the 1963 values of the Commission on Atomic Weights.

The group designations used here are the former Chemical Abstract Service numbers.

* Lanthanide Series

58 Ce 140.12	59 Pr 140.907	60 Nd 144.24	61 Pm (147)	62 Sm 150.35	63 Eu 151.96	64 Gd 157.25	65 Tb 158.924	66 Dy 162.50	67 Ho 164.930	68 Er 167.26	69 Tm 168.934	70 Yb 173.04	71 Lu 174.97

‡ Actinide Series

90 Th 232.038	91 Pa (231)	92 U 238.03	93 Np (237)	94 Pu (242)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (249)	99 Es (254)	100 Fm (253)	101 Md (256)	102 No (256)	103 Lr (257)

ATON PHARMA

SYPRINE

Dirty Bomb

Known Very Strongly Binding

Known Less Strongly Binding

PERIODIC CHART OF THE ELEMENTS

IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIII		IB	IIB	IIIA	IVA	VA	VIA	VIIA	INERT GASES
1 H 1.00797															1 H 1.00797	2 He 4.0026
3 Li 6.939	4 Be 9.0122										5 B 10.811	6 C 12.0112	7 N 14.0067	8 O 15.9994	9 F 18.9984	10 Ne 20.183
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19 K 39.102	20 Ca 40.08	21 Sc 44.956	22 Ti 47.90	23 V 50.942	24 Cr 51.996	25 Mn 54.9380	26 Fe 55.847	27 Co 58.9332	28 Ni 58.71	29 Cu 63.54	30 Zn 65.37	31 Ga 69.72	32 Ge 72.59	33 As 74.9216	34 Se 78.96	35 Br 79.909	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.905	40 Zr 91.22	41 Nb 92.906	42 Mo 95.94	43 Tc (99)	44 Ru 101.07	45 Rh 102.905	46 Pd 106.4	47 Ag 107.870	48 Cd 112.40	49 In 114.82	50 Sn 118.69	51 Sb 121.75	52 Te 127.60	53 I 126.904	54 Xe 131.30
55 Cs 132.905	56 Ba 137.34	*57 La 138.91	72 Hf 178.49	73 Ta 180.948	74 W 183.85	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.09	79 Au 196.967	80 Hg 200.59	81 Tl 204.37	82 Pb 207.19	83 Bi 208.980	84 Po (210)	85 At (210)	86 Rn (222)
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ATON PHARMA

Commercial Supplies of Penicillamine are Limited
Scaled to Demand of Current Market

- All US penicillamine sales in 2006 (Merck, Aton & Medpointe) were 2,802,981 doses (80% Merck/Aton)
- Aton current production:
  - Batch size: ≈ 340,000 capsules
  - Production lead time: 73 days
  - Annual production volume: ≈ 4.5 M capsules (2.4 M for US)
- Label initial dosing is 3-6 doses/day
- Assuming 3-6 doses x 28 days = 84-168 doses per course for acute radioisotope exposure, 3 mo Aton US inventory would treat:

  2,400,000 x 3 mo/12 mo = 600,000 doses in inventory

  600,000 / 84-168 doses per course ≈ 3,500-7,000 courses available on an emergency basis
- Other considerations
  - API supply constraints, ex-US source
  - Transition to contract manufacturing means less excess capacity

ATON PHARMA

Commercial Supplies of Trientine are Lower
Scaled to Lower Demand

- All US trientine sales in 2006 (Merck & Aton) were 584,880 doses
- Aton current production:
  - Batch size: ≈ 74,000 capsules
  - Production lead time: 60 days
  - Annual production volume: ≈ 1.5 M capsules (0.75 M for US)
- Label initial dosing is 4-8 doses/day
- Assuming 4-8 doses x 28 days = 112-224 doses per course for acute radioisotope exposure, 3 mo Aton US inventory would treat:

  750,000 x 3 mo/12 mo ≈ 190,000 doses in inventory

  190,000 / 112-224 doses per course ≈ 850-1,700 courses available on an emergency basis
- Other considerations
  - API supply constraints (lead time 11 months), US source
  - Cold storage (2-8^{o} C) required
  - Transition to contract manufacturing means less excess capacity

ATON PHARMA

Rationale for Stockpiling

- Cuprimine® and Syprine® are useful decorporation agents
  - REMM lists, and Los Angeles stockpiles, Cuprimine®
  - Animal (and some human) efficacy of Cuprimine® for ^{60}Co
  - Syprine® covers complementary set of metals
- Cuprimine® is a declining product, and may become commercially non-viable
- API sourcing is constrained, but would respond favorably with larger volumes
- Neither product is currently available commercially in large enough quantities to handle a substantial contamination event, nor can be made quickly on an emergency basis
- Stockpiling is justified
  - Provide emergency management workers with sufficient supplies to handle a crisis
  - Allow Aton to improve the supply chain

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