FUTURE ONCOLOGY

TECHNOLOGY, PRODUCTS, MARKETS AND SERVICE OPPORTUNITIES

A NEW MEDICINE PUBLICATION VOLUME 1, NUMBER 1-12 INDEX MAY 1996

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FUTURE ONCOLOGY STAFF:

PUBLISHER AND EDITOR: **Katie Siafaca, MS**
EPIDEMIOLOGY: **Anita Valabhji, MPH**
RESEARCH ASSOCIATES: **Sarah Nghiem and Fred Hall**
DESIGN & PRODUCTION: **Jill Burch**

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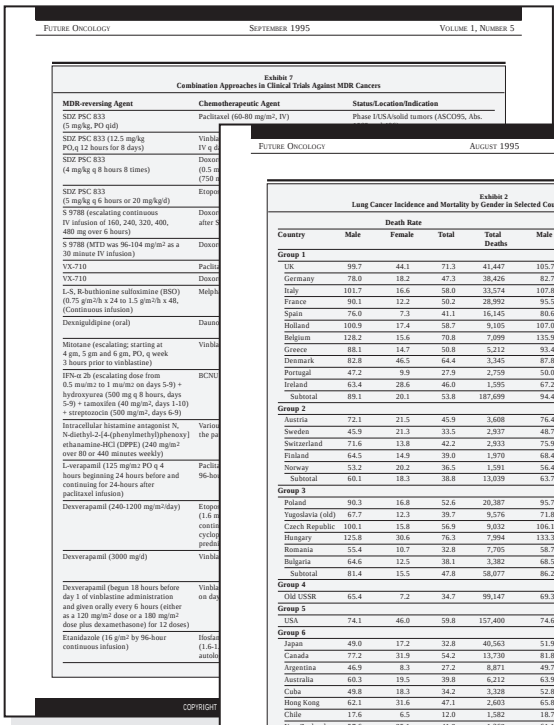
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Exhibit 7
Combination Approaches in Clinical Trials Against MDR Cancers

MDR-reversing Agent	Chemotherapeutic Agent	Status/Location/Indication
SDZ PSC 833 (5 mg/kg, PO qid)	Paclitaxel (60-80 mg/m2, IV)	Phase I/USA/solid tumors (ASCO95, Abs.
SDZ PSC 833 (12.5 mg/kg PO,q 12 hours for 8 days)	Vinbla IV q d	
SDZ PSC 833 (4 mg/kg q 8 hours 8 times)	Doxor (0.5 m (750 m	
SDZ PSC 833 (5 mg/kg q 6 hours or 20 mg/kg/d)	Etopo	
S 9788 (escalating continuous IV infusion of 160, 240, 320, 400, 480 mg over 6 hours)	Doxor after 5	
S 9788 (MTD was 96-104 mg/m2 as a 30 minute IV infusion)	Doxor	
VX-710	Paclita	
VX-710	Doxor	
L-S, R-buthionine sulfoximine (BSO) (0.75 g/m2/h x 24 to 1.5 g/m2/h x 48, (Continuous infusion)	Melph	
Dexniguldipine (oral)	Daunc	
Mitotane (escalating; starting at 4 gm, 5 gm and 6 gm, PO, q week 3 hours prior to vinblastine)	Vinbla	
IFN-α 2b (escalating dose from 0.5 mu/m2 to 1 mu/m2 on days 5-9) + hydroxyurea (500 mg q 8 hours, days 5-9) + tamoxifen (40 mg/m2, days 1-10) + streptozocin (500 mg/m2, days 6-9)	BCNU	
Intracellular histamine antagonist N, N-diethyl-2-[4-(phenylmethyl)phenoxy] ethanamine-HCl (DPPE) (240 mg/m2 over 80 or 440 minutes weekly)	Various the pa	
L-verapamil (125 mg/m2 PO q 4 hours beginning 24 hours before and continuing for 24-hours after paclitaxel infusion)	Paclita 96-ho	
Dexverapamil (240-1200 mg/m2/day)	Etopo (1.6 m contin cyclop predn	
Dexverapamil (3000 mg/d)	Vinbla	
Dexverapamil (bogus 18 hours before day 1 of vinblastine administration and given orally every 6 hours (either as a 120 mg/m2 dose or a 180 mg/m2 dose plus dexamethasone) for 12 doses)	Vinbla on da	
Etanidazole (16 g/m2 by 96-hour continuous infusion)	Ifosfa (1.6-1 autolo	

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Exhibit 2
Lung Cancer Incidence and Mortality by Gender in Selected Countries Worldwide in 1995

	Death Rate				Incidence Rate			
Country	Male	Female	Total	Total Deaths	Male	Female	Total	Total Incidence
Group 1								
UK	99.7	44.1	71.3	41,447	105.7	52.9	78.8	45,763
Germany	78.0	18.2	47.3	38,426	82.7	21.8	51.4	41,795
Italy	101.7	16.6	58.0	33,574	107.8	19.9	62.6	36,280
France	90.1	12.2	50.2	28,992	95.5	14.6	54.1	31,237
Spain	76.0	7.3	41.1	16,145	80.6	8.8	44.1	17,317
Holland	100.9	17.4	58.7	9,105	107.0	20.9	63.5	9,842
Belgium	128.2	15.6	70.8	7,099	135.9	18.7	76.1	7,637
Greece	88.1	14.7	50.8	5,212	93.4	17.6	54.9	5,632
Denmark	82.8	46.5	64.4	3,345	87.8	55.8	71.6	3,717
Portugal	47.2	9.9	27.9	2,759	50.0	11.9	30.3	2,995
Ireland	63.4	28.6	46.0	1,595	67.2	34.3	50.7	1,760
Subtotal	89.1	20.1	53.8	187,699	94.4	24.1	58.4	203,975
Group 2								
Austria	72.1	21.5	45.9	3,608	76.4	25.8	50.2	3,947
Sweden	45.9	21.3	33.5	2,937	48.7	25.6	37.0	3,246
Switzerland	71.6	13.8	42.2	2,933	75.9	16.6	45.7	3,178
Finland	64.5	14.9	39.0	1,970	68.4	17.9	42.4	2,142
Norway	53.2	20.2	36.5	1,591	56.4	24.2	40.2	1,749
Subtotal	60.1	18.3	38.8	13,039	63.7	22.0	42.4	14,261
Group 3								
Poland	90.3	16.8	52.6	20,387	95.7	20.2	57.0	22,078
Yugoslavia (old)	67.7	12.3	39.7	9,576	71.8	14.8	43.0	10,361
Czech Republic	100.1	15.8	56.9	9,032	106.1	19.0	61.4	9,753
Hungary	125.8	30.6	76.3	7,994	133.3	36.7	83.1	8,707
Romania	55.4	10.7	32.8	7,705	58.7	12.8	35.5	8,346
Bulgaria	64.6	12.5	38.1	3,382	68.5	15.0	41.2	3,665
Subtotal	81.4	15.5	47.8	58,077	86.2	18.6	51.7	62,908
Group 4								
Old USSR	65.4	7.2	34.7	99,147	69.3	8.6	37.3	106,619
Group 5								
USA	74.1	46.0	59.8	157,400	74.6	54.8	64.6	169,900
Group 6								
Japan	49.0	17.2	32.8	40,563	51.9	20.6	36.0	44,511
Canada	77.2	31.9	54.2	13,730	81.8	38.3	59.8	15,127
Argentina	46.9	8.3	27.2	8,871	49.7	10.0	29.4	9,596
Australia	60.3	19.5	39.8	6,212	63.9	23.4	43.6	6,798
Cuba	49.8	18.3	34.2	3,328	52.8	22.0	37.5	3,651
Hong Kong	62.1	31.6	47.1	2,603	65.8	37.9	52.1	2,879
Chile	17.6	6.5	12.0	1,582	18.7	7.8	13.1	1,738
New Zealand	57.6	25.1	41.2	1,362	61.1	30.1	45.4	1,503
Uruguay	83.8	7.3	44.6	1,317	88.8	8.8	47.8	1,411
Singapore	42.2	16.3	29.4	796	44.7	19.6	32.3	874
Israel	27.8	10.7	19.2	776	29.5	12.8	21.1	853
Costa Rica	11.1	5.5	8.3	201	11.8	6.6	9.2	222

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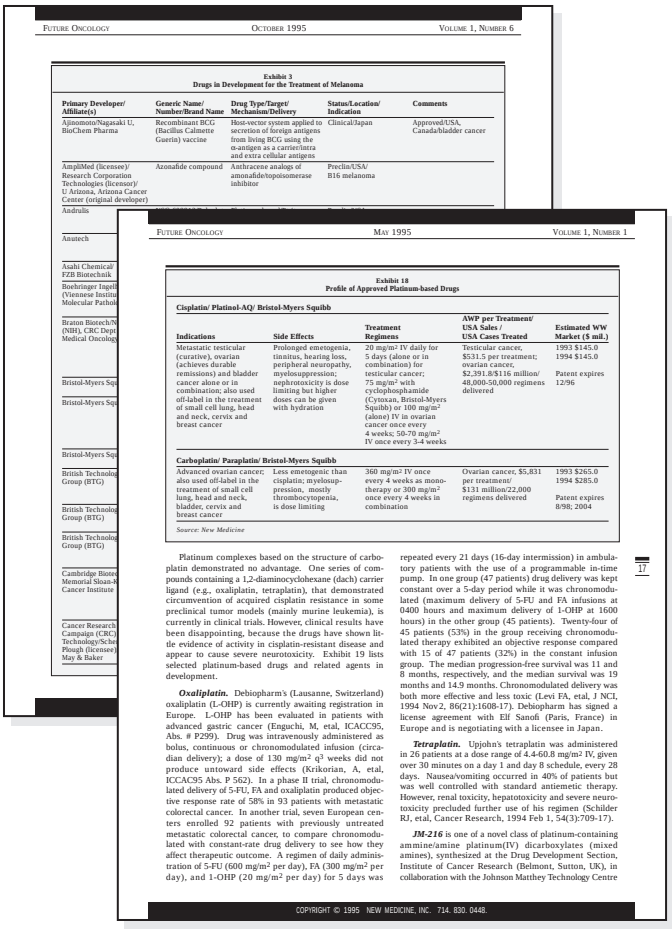
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Exhibit 3
Drugs in Development for the Treatment of Melanoma

Primary Developer/ Affiliate(s)	Generic Name/ Number/Brand Name	Drug Type/Target/ Mechanism/Delivery	Status/Location/ Indication	Comments
Ajinomoto/Nagasaki U, BioChem Pharma	Recombinant BCG (Bacillus Calmette Guerin) vaccine	Host-vector system applied to secretion of foreign antigens from living BCG using the α-antigen as a carrier/intra and extra cellular antigens	Clinical/Japan	Approved/USA, Canada/bladder cancer
AmpliMed (licensee)/ Research Corporation Technologies (licensor)/ U Arizona, Arizona Cancer Center (original developer)	Azonafide compound	Anthracene analogs of amonafide/topoisomerase inhibitor	Preclin/USA/ B16 melanoma	
Andrulis				
Anutech				
Asahi Chemical/ FZB Biotechnik				
Boehringer Ingell (Viennese Institu Molecular Pathol				
Braton Biotech/N (NIH), CRC Dept Medical Oncolog				
Bristol-Myers Squ				
Bristol-Myers Squ				
Bristol-Myers Squ				
British Technolog Group (BTG)				
British Technolog Group (BTG)				
British Technolog Group (BTG)				
Cambridge Biote Memorial Sloan-K Cancer Institute				
Cancer Research Campaign (CRC) Technology/Sche Plough (licensee) May & Baker				

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Exhibit 18
Profile of Approved Platinum-based Drugs

Cisplatin/ Platinol-AQ/ Bristol-Myers Squibb

Indications	Side Effects	Treatment Regimens	AWP per Treatment/ USA Sales / USA Cases Treated	Estimated WW Market ($ mil.)
Metastatic testicular (curative), ovarian (achieves durable remissions) and bladder cancer alone or in combination; also used off-label in the treatment of small cell lung, head and neck, cervix and breast cancer	Prolonged emetogenia, tinnitus, hearing loss, peripheral neuropathy, myelosuppression; nephrotoxicity is dose limiting but higher doses can be given with hydration	20 mg/m2 IV daily for 5 days (alone or in combination) for testicular cancer; 75 mg/m2 with cyclophosphamide (Cytoxan, Bristol-Myers Squibb) or 100 mg/m2 (alone) IV in ovarian cancer once every 4 weeks; 50-70 mg/m2 IV once every 3-4 weeks	Testicular cancer, $531.5 per treatment; ovarian cancer, $2,391.8/$116 million/ 48,000-50,000 regimens delivered	1993 $145.0 1994 $145.0 Patent expires 12/96

Carboplatin/ Paraplatin/ Bristol-Myers Squibb

Advanced ovarian cancer; also used off-label in the treatment of small cell lung, head and neck, bladder, cervix and breast cancer	Less emetogenic than cisplatin; myelosuppression, mostly thrombocytopenia, is dose limiting	360 mg/m2 IV once every 4 weeks as monotherapy or 300 mg/m2 once every 4 weeks in combination	Ovarian cancer, $5,831 per treatment/ $131 million/22,000 regimens delivered	1993 $265.0 1994 $285.0 Patent expires 8/98; 2004

Source: New Medicine

Platinum complexes based on the structure of carboplatin demonstrated no advantage. One series of compounds containing a 1,2-diaminocyclohexane (dach) carrier ligand (e.g., oxaliplatin, tetraplatin), that demonstrated circumvention of acquired cisplatin resistance in some preclinical tumor models (mainly murine leukemia), is currently in clinical trials. However, clinical results have been disappointing, because the drugs have shown little evidence of activity in cisplatin-resistant disease and appear to cause severe neurotoxicity. Exhibit 19 lists selected platinum-based drugs and related agents in development.

Oxaliplatin. Debiopharm's (Lausanne, Switzerland) oxaliplatin (L-OHP) is currently awaiting registration in Europe. L-OHP has been evaluated in patients with advanced gastric cancer (Enguchi, M, etal, ICACC95, Abs. # P299). Drug was intravenously administered as bolus, continuous or chronomodulated infusion (circadian delivery); a dose of 130 mg/m2 q3 weeks did not produce untoward side effects (Krikorian, A, etal, ICCAC95 Abs. P 562). In a phase II trial, chronomodulated delivery of 5-FU, FA and oxaliplatin produced objective response rate of 58% in 93 patients with metastatic colorectal cancer. In another trial, seven European centers enrolled 92 patients with previously untreated metastatic colorectal cancer, to compare chronomodulated with constant-rate drug delivery to see how they affect therapeutic outcome. A regimen of daily administration of 5-FU (600 mg/m2 per day), FA (300 mg/m2 per day), and 1-OHP (20 mg/m2 per day) for 5 days was repeated every 21 days (16-day intermission) in ambulatory patients with the use of a programmable in-time pump. In one group (47 patients) drug delivery was kept constant over a 5-day period while it was chronomodulated (maximum delivery of 5-FU and FA infusions at 0400 hours and maximum delivery of 1-OHP at 1600 hours) in the other group (45 patients). Twenty-four of 45 patients (53%) in the group receiving chronomodulated therapy exhibited an objective response compared with 15 of 47 patients (32%) in the constant infusion group. The median progression-free survival was 11 and 8 months, respectively, and the median survival was 19 months and 14.9 months. Chronomodulated delivery was both more effective and less toxic (Levi FA, etal, J NCI, 1994 Nov 2, 86(21):1608-17). Debiopharm has signed a license agreement with Elf Sanofi (Paris, France) in Europe and is negotiating with a licensee in Japan.

Tetraplatin. Upjohn's tetraplatin was administered in 26 patients at a dose range of 4.4-60.8 mg/m2 IV, given over 30 minutes on a day 1 and day 8 schedule, every 28 days. Nausea/vomiting occurred in 40% of patients but was well controlled with standard antiemetic therapy. However, renal toxicity, hepatotoxicity and severe neurotoxicity precluded further use of his regimen (Schilder RJ, etal, Cancer Research, 1994 Feb 1, 54(3):709-17).

JM-216 is one of a novel class of platinum-containing ammine/amine platinum(IV) dicarboxylates (mixed amines), synthesized at the Drug Development Section, Institute of Cancer Research (Belmont, Sutton, UK), in collaboration with the Johnson Matthey Technology Centre

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