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INDUSTRY UPDATE NOTE

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Sector Analysis, Initiating Dawson James Sector Indices: Rare Diseases/Neuro-oncology

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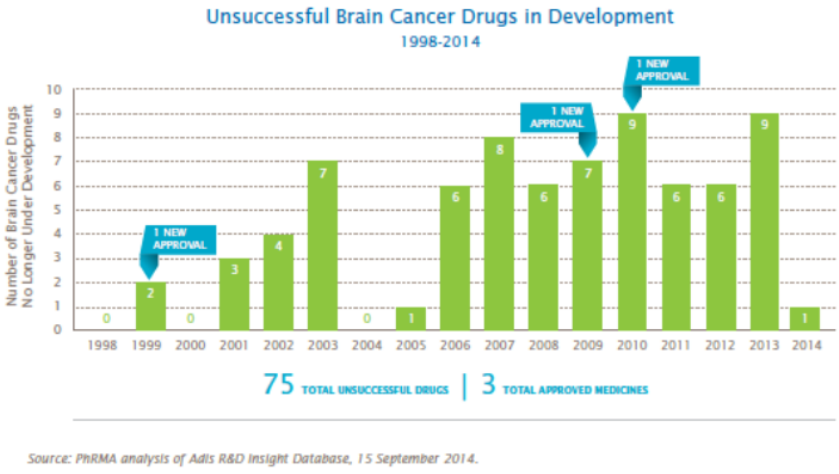
In our December 2015 introduction to comparative biology explaining the premise behind the NIH's formalization of the Comparative Oncology Trial Consortium Program (COTP), we highlighted some discouraging statistics concerning neurological (glioma) cancers. This specific indication is one that has particularly facilitated the collaborations embodied in the COPT. The incidence rate of all primary malignant brain and central nervous system tumors is 7.4 per 100,000 person-years or about 22,000-25,000 new cases of primary brain malignancies diagnosed annually in the US, according to the NCI. For glioblastoma multiforma (GBM), which constitutes about 70% of malignant gliomas, the 5-year survival rate is 14% for 20-44 year olds and only 1% for 55-64 year old patients (Source: University of Maryland Medical Center website). Nothing states the problem more succinctly then the accompanying chart.

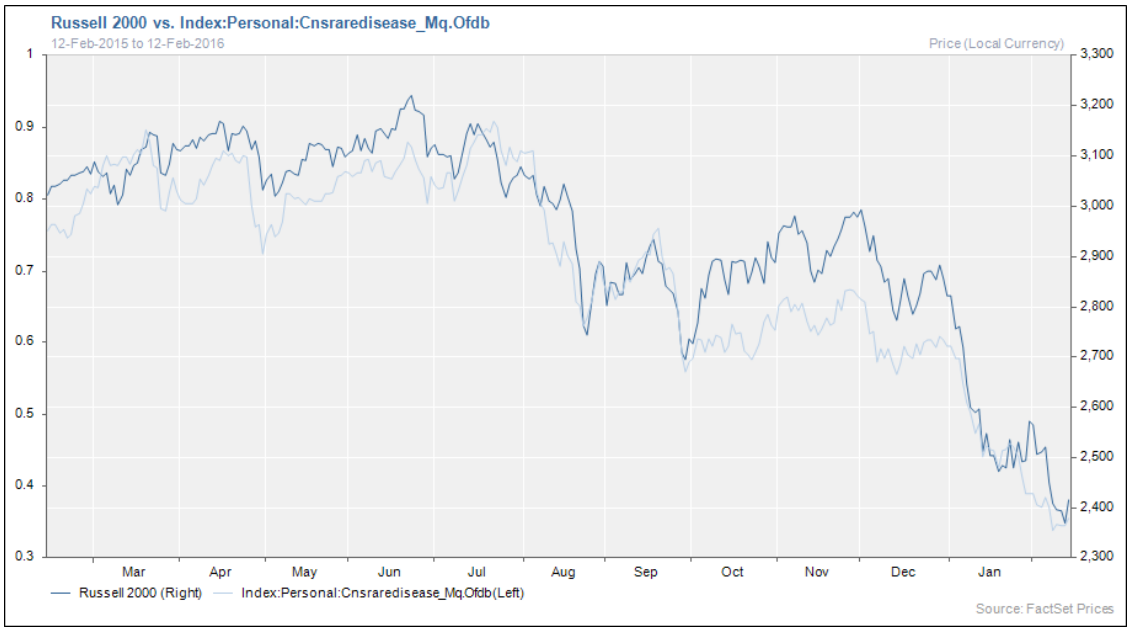


Source: PhRMA analysis of Adis R&D Insight Database, 15 September 2014.

The lack of treatment progress in this indication cannot be overstated as only Avastin and Ceenu (lomustine) have received FDA approval for the treatment of brain cancer (malignant glioma) since the 1999 approval of Merck's Temodar (temozolomide or TMZ), the current "gold standard". Novartis alone has tried with 12 different drugs, five of which had their clinical trial programs suspended. Ineffective drug delivery across the blood-brain barrier or within the brain itself, high adverse event profiles, and the tendency for gliomal tumor escape due to drug resistance, contribute to the technical difficulties facing drug developers in this indication. As a result, of rare cancers, brain cancer is seeing an unusually wide variety of technological approaches to treatment, including radiation combination strategies, gene-based therapeutics, immunotherapy, molecularly-targeted therapies, angiogenesis inhibitors and the use of devices as therapeutics or in combination with drugs—in other words, everything including the "kitchen sink" is being tried. We have identified over 20 public companies, primarily US-based, along with a number of private companies that are pursuing the development of novel treatments for a variety of neurological and CNS-related cancers. Some are actively employing comparative oncology in their translational and clinical trial research strategies. A number of companies will be reporting significant clinical events during 2016, and thus, warrant investor focus.

Please find Important Disclosures beginning on Page 7.

DAWSON JAMES CNS RARE DISEASE INDEX



DAWSON JAMES CNS RARE DISEASE INDEX COMPANIES

Ticker	Security Name	Last*	%Chg	30 Day Vol Avg	Day Day Vol	YTD %Chg	12 Mo 12Mo %Chg	Mkt Cap ($MM's)	EPS FY1	PE FY1
ADRO	Aduro BioTech, Inc.	14.97	4.61%	352,187	265,645	-46.80%	--	905	-1.06	--
AGEN	**Agenus Inc. ****	3.01	6.36%	1,354,347	829,315	-33.70%	-40.16%	244	-1.05	--
AGIO	Agios Pharmaceuticals, Inc.	39.76	5.30%	1,040,448	669,414	-38.76%	-66.46%	1,421	-2.60	--
ARIA	ARIAD Pharmaceuticals, Inc.	4.86	2.97%	3,920,496	2,609,265	-22.24%	-33.88%	893	-1.26	--
BINV-OME	BioInvent International AB	2.69	2.67%	576,299	351,562	-29.02%	14.09%	427	-0.58	--
CALA	Calithera Biosciences, Inc.	5.59	10.04%	170,894	89,601	-27.02%	-65.30%	92	-1.92	--
CLDX	Celldex Therapeutics, Inc.	7.69	6.07%	3,303,176	3,724,345	-50.96%	-63.33%	715	-1.32	--
CTIC	CTI BioPharma Corp.	0.42	22.91%	3,042,459	5,093,424	-66.11%	-81.31%	95	-0.60	--
CYTR	CytRx Corporation	2.77	10.80%	549,173	1,855,040	4.53%	-6.42%	166	-0.79	--
DMPI	DelMar Pharmaceuticals, Inc.	0.81	5.18%	19,748	34,866	-13.84%	15.70%	30	-0.15	--
DFFN	Diffusion Pharmaceuticals Inc.	1.24	-0.64%	9,173	3,066	24.20%	-58.60%	23	--	--
ETX-LON	e-Therapeutics plc	0.22	0.00%	62,251	223,508	-21.10%	-35.82%	69	--	--
EXEL	Exelixis, Inc.	4.22	0.48%	4,944,196	6,496,997	-25.18%	70.16%	954	-0.85	--
GNSZ	GenSpera, Inc.	0.14	-3.52%	36,679	63,805	-9.74%	-85.27%	6	-0.17	--
GWP-LON	GW Pharmaceuticals PLC	2.65	0.38%	556,624	632,444	-33.23%	-35.82%	651	-0.32	--
IMUC	ImmunoCellular Therapeutics, Lt	0.24	7.31%	305,453	164,090	-32.62%	-55.67%	20	-0.14	--
IMV-TSE	Immunovaccine Inc.	0.49	6.52%	46,160	11,050	-33.78%	-28.99%	42	--	--
INSY	Insys Therapeutics, Inc.	17.68	4.06%	995,243	364,854	-38.25%	-31.34%	1,224	1.31	13.44
KPTI	Karyopharm Therapeutics, Inc.	5.83	5.05%	393,320	291,399	-56.00%	-78.50%	198	-3.21	--
KITE	Kite Pharma, Inc.	44.89	4.69%	1,325,308	1,004,656	-27.15%	-28.28%	2,041	-1.92	--
NLNK	Newlink Genetics Corporation	22.19	5.42%	549,159	379,857	-39.02%	-42.87%	606	-1.55	--
NWBO	Northwest Biotherapeutics, Inc.	2.31	17.26%	458,375	383,681	-27.81%	-61.94%	189	--	--
ONC-TSE	Oncolytics Biotech Inc.	0.38	2.70%	49,670	95,470	-1.30%	-39.68%	44	-0.13	--
OXGN	OXiGENE, Inc.	0.5	-7.41%	155,389	65,593	-34.20%	-68.94%	14	-0.53	--
PPHM	Peregrine Pharmaceuticals, Inc.	0.92	2.22%	1,196,099	542,764	-21.37%	-28.12%	207	-0.29	--
STML	Stemline Therapeutics, Inc.	4.64	8.41%	92,649	50,152	-26.47%	-67.02%	77	-2.12	--
TCON	TRACON Pharmaceuticals, Inc.	6.59	2.09%	42,979	17,070	-28.68%	-29.44%	79	-1.85	--
VBLT	Vascular Biogenics Ltd.	3.17	2.59%	155,869	49,546	-39.73%	-77.53%	69	-0.87	--
ZIOP	ZIOPHARM Oncology, Inc.	6.12	9.29%	3,126,514	2,292,494	-26.35%	-36.51%	733	-0.97	--

Source: FactSet

*Prices intraday 2/16/16

** Agenus Inc. (AGEN/Rated Neutral)

As is the case with our Dawson James Molecular Diagnostics Index, we have chosen to eliminate selected large cap companies, and in particular for this index, "Big Pharma". We believe by doing so we have focused our sector on what we believe are the real "innovators". Two companies, Calithera Biosciences and Diffusion Pharmaceuticals are newcomers to the public market as they both completed pubco reverse mergers since January 1st. We have also chosen to benchmark the index to the Russell 2000, which in this case, is very highly correlated with the Index. Of note is the fact that the Russell 2000 appears to be making a slight upward move in the last week or so, which may foreshadow an improvement in price action for this entire group.

Selected Comparative Oncology Clinical Work From Our Subsector Companies

With regard to specific work in neurological cancers, of the 25 or more US veterinary research institutions employing comparative biology, several are actively involved with clinical research in gliomas and other neuro cancers. These include Texas A&M, the Animal Medical Center in New York City, Purdue University's Comparative Center for Translational Research, UC Davis Comparative Cancer Center, the University of Minnesota and the University of Illinois, to name a few. In January, the list was expanded with the formation of the Comparative Medicine Institute, a collaboration among North Carolina State University, University of North Carolina –Chapel Hill and Duke University. The Comparative Medicine Institute will hold its inaugural scientific symposium on March 4, 2016.

Human neurological cancer studies typically can have very long trial periods, especially in novel Phase I or Phase I/II trials, with some listed on ClinicalTrials.gov as taking as long as 6-10 years before trial completion. The complexity of new treatment strategies and protocols make neurological cancers a valuable model of the comparative oncology approach, where first-in-man or first-in-class treatments and treatment combinations can be tested and used to inform human counterpart clinical trials at early time points. Furthermore, the incidence of primary brain tumors in animals is actually higher than that of humans. Surveys of necropsy data suggest that the incidence is in the region of 10-20 per 100,000 animals, or 1-3% of all deaths where necropsy was done. Recall that the incidence of primary malignant brain tumors in people is approximately 7 individuals per 100,000. Primary nervous system tumors in dogs account for 60-80% of all such tumors reported in domestic animals (10-20% in cats; 10-20% in other species). Brachycephaly, a head geometry trait characterized by a short muzzle and wide head, is closely associated with canine brain tumors and respiratory problems. This trait is found in several breeds, including Boxers, Bulldogs, and Boston Terriers and its genetics are being studied for its indication of a heightened risk for gliomas in dogs, and as a possible biomarker for humans.

We have identified several interesting examples of comparative neuro-oncology in practice:

The University of Minnesota has established the Canine Brain Tumor Clinical Trial Program specifically to take information from canine brain cancer trials and translate it into human clinical trial design. Of note is that the majority of the costs associated with these experimental brain tumor therapies is paid for by grants from both human and animal foundation and government agencies, including the Children's Cancer Research Fund, the Randy Shaver Cancer Research and Community Fund, the National Institutes of Health, the American Cancer Society, the American Brain Tumor Association and the American Kennel Club Canine Health Foundation.

In a novel delivery system approach, UC Davis School of Veterinary Medicine partnered with UC San Francisco Department of Neurosurgery to collaborate for a clinical trial undertaken to investigate the efficacy of liposomal CPT-11 (camptothecin or "Irinotecan", a topoisomerase I inhibitor), administered directly into gliomas using a novel Convection Enhanced Delivery (CED) system, originally developed by the NIH to

improve drug targeting to brain cancer. The treatment was monitored in real-time using co-infusion of a gadolinium marker and MRI.

Data from canine-diagnosed gliomas suggested that real-time imaging in future CED clinical trials (canine or human) was essential in order to define early leakage of infusates to non-target tissues, thus allowing modification of infusions during the canine trial and tracking of corresponding response to therapy. Therapeutic response, defined by decrease in tumor volume (up to 80%), and modification of tumor phenotype (decreased Mib-1 index in infused vs non-infused tumor based on histopathology) as well as documented adverse effects also provided additional clinically relevant data for the development of intratumoral liposomal CPT-11 as a potential therapy in human gliomas.

NeoPharm, Inc, now INSYS Therapeutics, Inc. (INSY/ $17.52/Not rated), completed a Phase I clinical trial in 2010 based on these studies. *"Liposome Encapsulated SN38 (LE-SN38) is an oncology drug product consisting of the active metabolite of irinotecan (CPT-11), a known anticancer drug, encapsulated in a liposome. Formulation of a relatively insoluble compound (SN38) and improvement in drug delivery (pharmacodynamic profile) may be obtained with liposomal formulations. An improved safety and efficacy profile, compared with the pro-drug CPT-11 may be possible. This rationale is supported by the results from animal toxicity studies in both the mouse and dog."* (Source: www.clinicaltrials.gov, **ClinicalTrials.gov Identifier:NCT00046540**, INSYS Therapeutics)

Peregrine Pharmaceuticals, Inc. (PPHM/$1.00/Not rated) is also employing the CED delivery technology. The Company's lead neuro-oncology product, **Cotara**, is a novel combination therapy that conjugates a radioactive isotope to a monoclonal antibody designed to target and bind to the DNA histone H1 complex, necessary for cell division, that is exposed by necrotic cells at the center of a tumor. The radioactive payload is delivered to adjacent live cells, and the tumor is effectively "radioactively burned" from the inside to the outside of the tumor. Cotara is administered as a single CED dose. Cotara successfully completed Phase II trials in 2011 and Peregrine states on its website, further clinical development of Cotara is contingent upon funding, licensing or a development partner while Peregrine pursues other immune-oncology candidates in breast, lung and other solid tumor cancers. The Virginia-Maryland Regional College of Veterinary Medicine continues to conduct molecular combination therapy trials for canine glioma patients using the CED delivery system.

Washington State University and City of Hope Medical Center (Los Angeles) are both researching the use of the precursor drug, 5-fluorocytosine (FC) delivered in combination with gene therapy as new treatment paradigm for gliomas. 5-FC is converted to the chemotherapy agent 5-FU (fluorouracil) at tumor sites in situ by e. coli CD-expressing genetically-modified neural stem cells (NSCs). Both canine and human patients received intracerebral injection of the genetically modified cells, followed by oral doses of 5-FC. In this case, Washington State University is using a human therapy approach for better drug delivery in dogs with gliomas.

Tocagen, Inc., a private company based in San Diego, received a $200,000 grant from the American Brain Tumor Association (ABTA) in 2011 to support the evaluation of its investigational combination 5FC prodrug treatment comprised of Toca 511 & Toca FC in companion dogs with malignant glioma. The study results were applied to improve the delivery methods and dose optimization in the human clinical trials. In the human clinical trials, Tocagen's investigational drug Toca 511, the first component of the two-part anti-tumor regimen, is injected into the tumor. Toca 511 is a retrovirus designed to spread selectively in cancer cells, carrying a gene to activate the second part of the therapy, an investigational formulation of 5-FC called Toca FC. Within Toca 511-infected cancer cells, the gene produces an enzyme which converts 5-FC into the anti-cancer drug 5-FU. The Toca 511/Toca FC combination is currently in a 170-patient active-comparator Phase II/III trial against Standard of Care (SOC) (TMZ, Avastin, CCNU) at 10 centers in the US, according to ClinicalTrials.gov, and is expected to be completed in 2019.

News in 2016 Will Drive Investor Interest

We expect that the innovators in our sector will drive renewed investor interest in neuro-oncology. The lack of any successful approvals in recent years opens the door to a unique opportunity for one of these companies' technologies to become truly transformative for patients with brain cancers. Out of the universe of companies in our subsector, only four of these public companies, Celldex Therapeutics, Inc. (CLDX/$6.91/Not rated), Immuocellular Therapeutics, Inc. (IMUC/$0.25/ Not rated), Northwest Biotherapeutics, Inc. (NWBO/$2.40/Not rated) and VBL (Vascular Biogenics Ltd.) Therapeutics (VBLT/$3.30/Not rated) are in Phase III trials. Over half of the remainder of our universe is either in the transition from Phase I to Phase II or completing Phase II clinical trials. This should bode well for a relative high level of news and clinical events for the sector for 2016.

Here are the Phase III companies that we believe will help drive the sector during 2016:

Celldex has seen much volatility since January 1 as investors take sides as to the nature of the upcoming interim results for its pivotal Phase III –ACT IV trial for RINTEGA®, an immunotherapy product comprised of rindopepimut and GM-CSF in combination with adjuvant TMZ. Investors had responded favorably to Phase II data reported at the Society of Neuro-oncology (SNO) last fall based in part due to a positive trend in the "p value" compared to prior reported results. However, since the beginning of the year, investors have punished the stock ahead of the upcoming second interim results, due to be reported at almost any time this quarter. The ACT-IV trial is large, with over 700 patients enrolled, and is directed to EGFRv3-positive glioblastoma patients. EGFRv-3 is expressed in about 30% of GBM tumors. Rindopepimut consists of a EGFRv3 targeting peptide conjugated to a keyhole limpet hemocyanin (KLH) immunostimulant carrier.

Northwest Bio, a dendritic cell immunotherapy company, has also seen its shares plummet in recent weeks. The Company's Phase III GBM pivotal trial for DC-Vax-L, an autologous dendritic cell product pulsed with tumor lysate antigen, completed enrollment in October 2015. The trial enrolled 348 newly diagnosed GBM patients at 85 US and x-US sites and is expected to be completed in September 2016. This is a placebo-controlled, DC-Vax-L+SOC (radiation +TMZ) trial. News on the company suggests that some investors may be watching for the possibility of an outsized placebo effect, which could impact final results.

Immunocellular, a stem cell immunotherapy company, just initiated enrollment in its Phase III trial for ICT-107. ICT-107 is also an autologous dendritic cell-derived immunotherapy that activates antigen-specific killer T-cells. ICT-107 incorporates six tumor-associated antigens and addresses the newly diagnosed GBM HLA-A2 patient population. A follow-on product, ICT-121, a CD133 stem cell antigen/dual epitope therapy, is being developed for recurrent GBM HLA-2 patients. Following favorable overall survival benefit found in the Phase II trial for specific HLA subgroups, the Phase III trial design was optimized with a few significant changes compared to the Phase II protocol. The double-blinded, placebo-controlled trial will enroll 400 HLA-A2 subgroup patients who will be further stratified according to individual immune status. Monocytes will replace dendritic cells as the placebo and iRANO criteria will be used at a central level to determine disease progression. The trial will span 120 sites in the US, Canada and Europe and is expected to take about two years to reach the futility interim analysis, modeled at 33% of events. Efficacy interim analysis is modeled at 60% of events. Patients are being stratified for MGMT, age and resection status. During 2016, IMUC is expected to report on enrollment status, site activation and Canadian and EU approvals to begin additional Phase III ICT-107 trial activity. News on ICT-121 will likely center on full enrollment being achieved in the second quarter of 2016.

VBL, another immunotherapy company, also reported favorable Phase II data for its lead therapy, VB-111, at the SNO meeting in the fall of 2015. VB-111 is a novel anti-angiogenesis viral vector gene technology used in combination with Avastin. The Phase II trial met its primary endpoint and doubled the survival rate in recurrent GBM (rGBM). The Company started its GLOBE rGBM pivotal Phase III in August 2015, an event-driven trial under a Special Protocol Assessment, Fast Track and Orphan designations. We would expect enrollment and interim "event" news concerning this trial during 2016, with trial results reported (depending upon the timing of events) in early 2017.

Among Phase II companies, we would look for market impacting news from the following:

DelMar Pharmaceuticals (DMPI/$0.77/Not rated) gave an extensive update to investors on the clinical progress of VAL-083 (dianhydrogalactitol) for refractory GBM during their year-end conference call on February 17th. VAL-083 is a unique treatment candidate in that it is a small molecule with a long history via the NCI. The drug is already approved in China to treat lung cancer and lymphoma. In fact, GBM clinical trials using dianhydrogalactitol can be found in the scientific literature going back as far as 1981. VAL-083 is currently in a dose optimized (40mg/m^2) Phase II expansion phase for patients refractory to TMZ and Avastin. 2016 will be a very important clinical year for DelMar with top line Phase II data expected in the first half of the year and FDA discussions to be initiated related to progressing to a Phase III registration-directed trial.

Importantly, DelMar is seeking to expand the indications for VAL-083 by taking advantage of its independence from MGMT resistance. VAL-083 is a bifunctional hexitol derivative that alkylates and cross-links DNA during all phases of the cell cycle, resulting in disruption of DNA function and cell cycle arrest. The novel mechanism of action, unlike any of the standard of care treatments, allows the drug to act independently of MGMT (O6-methylguanine DNA methyltransferase) which is a DNA repair mechanism known to contribute to the resistance of many gliomas to alkylating agents like TMZ. Markers for MGMT are now being used to better stratify responders to TMZ. The initial effort in this regard will be the initiation of a new Phase II study in 2016 in collaboration with MD Anderson to treat "recurrent-like, high MGMT-expression" GBM patients at the first recurrence/progression, ahead of Avastin. The Company intends to announce the initiation of other sub population-based VAL-083 trials during the course of the year, including one in refractory non-small cell lung cancer (NSCLC).

Diffusion Pharmaceuticals Inc. (DFFN/$1.24/Not rated), newly public through a reverse merger, is focused on a therapeutic strategy aimed at re-oxygenating highly hypoxic tumors, as is the case with GBM, in order to make the tumor microenvironment more amenable to standard of care treatments. The Company's lead product, trans sodium crocetinate (TSC) completed a Phase II trial with 59 newly diagnosed GBM patients in mid 2015 with median survival of 16.3 months and a two year survival rate of 36.3%. A single 65-site multi-national 400 patient Phase III 400 trial, supportive of registration, is expected to being enrollment in 2016. Other corporate announcements for 2016 include the initiation of a Phase II TSC trial for pancreatic cancer and a Phase II/III trial for metastatic brain cancer. The median survival of patients with brain metastases is three to six months, post radiation treatment.

Concluding Thoughts

2015 saw a resurgence of interest in neurological indications, both in the neuro-oncology arena and in neurodegenerative diseases, after a number of years of very high profile clinical failures and lack of progress. The new technologies and novel combination of technologies represented by this subgroup of companies is a testament to the conviction of researchers who have been hard at work during the period of investor apathy. We believe that, in many cases, companies in our subsector may represent unusual "value" plays at current levels.*SG*

Risk Factors

In addition to normal economic and market risk factors that impact most equities, and the common risks shared by the companies named in this sector and those in the biotechnology sector as a whole, we believe an investment in any of the Dawson James CNS Rare Disease Sector companies involves the following risks:

- **Regulatory risks** – the companies in the DJ CNS Rare Disease Sector are subject to regulatory review for their ongoing research and development activities and manufacturing operations with local, state and federal governmental agencies both in the US and Internationally.

- **Need to defend patents, trade secrets and other intellectual property** – Biotechnology companies rely heavily on intellectual property related to their technology and products. While larger companies may have adequate resources to defend their intellectual property, most of the smaller companies in the DJ CNS Rare Disease Sector would be materially and negatively impacted by intellectual property infringement or the loss of one or more patents.

- **Historical lack of profitability** – To date this year and in past years, most of the companies in the DJ CNS Rare Disease Sector have not operated on a profitable basis, and are not forecast to do so in the immediate future. Although companies typically have been able to raise funds from the capital markets, there can be no guarantee that any particular company will not be able raise additional operating capital in the future should losses continue.

- **Competitive Markets** – This universe of companies operate in a highly competitive marketplace, where speed to market, clinical results and other factors bear on a company's viability. There can be no assurance that any one company will be able to continue to market or later launch its products successfully in these competitive markets in the future.

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1) **Buy**: the analyst believes the price of the stock will appreciate and produce a total return of at least 20% over the next 12-18 months;
2) **Neutra**l: the analyst believes the price of the stock is fairly valued for the next 12-18 months;
3) **Sel**l: the analyst believes the price of the stock will decline by at least 20% over the next 12-18 months and should be sold.

The following chart reflects the range of current research report ratings for all companies followed by the analysts of the Firm. The chart also reflects the research report ratings relating to those companies for which the Firm has performed investment banking services.

	Company Coverage		Investment Banking	
Ratings Distribution	# of Companies	% of Total	# of Companies	% of Totals
Market Outperform (Buy)	16	67%	10	63%
Market Perform (Neutral)	8	33%	6	75%
Market Underperform (Sell)	0	0%	0	0%
Total	24	100%	16	67%

Analyst Certification:

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