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Biotechnology
Company Update
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BUY
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CONCERT PHARMACEUTICALS INC.

Progress with Avanir's AVP-786, and Recently With FDA for '354

CNCE (NASDAQ)

Company & Market Data	
Closing Price (as of July 18, 2014):	$8.24
Rating:	BUY
Price Target:	$24.00
52 Week Range:	$7.12 - $16.26
Shares Outstanding (MM):	18
Market Capitalization (MM):	$147
Cash (MM):	$108.0
Debt (MM):	$13.0
Fiscal Year End:	Dec

Estimates	2013A	2014E	2015E
EPS			
1Q	—	$(0.76)A	—
2Q	—	$(0.37)	—
3Q	—	$(0.38)	—
4Q	—	$(0.28)	—
Full Year	$(4.99)	$(1.61)	$(0.52)
Revenue (MM)	$25.4	$10.4	$27.5

Ratios			
P/E	NA	NA	NA

Concert Pharmaceuticals, founded in 2006 by Richard Aldrich, Roger Tung, and Christoph Westphal, creates novel medicines by applying its DCE (Deuterated Chemical Entity) Platform technologies to molecules. The DCE approach involves the selective addition of deuterium, a stable isotope of hydrogen, to molecules, resulting in clinical therapeutic candidates with improved pharmacology. This approach has the potential to enable more efficient drug discovery and clinical development. Concert's proprietary programs include CTP-354, a novel GABA-A modulator for spasticity and anxiety, and CTP-499, a PDE inhibitor for diabetic kidney disease. Promising partnered programs include Jazz's JZP-386, a long-acting Xyrem, Avanir's AVP-786, an improved Neudexta, and multiple programs with Celgene. Concert has also developed a broad portfolio of deuterated molecules that are expected to migrate into and through the clinic over time.

This note replaces an earlier version from today where AVP-786 was mislabeled.

Concert's Partnered AVP-786 Moves Into Phase 2 In Depression. Concert's collaborations for its deuteration technology include Avanir's AVP-786, a deuterated dextromethorphan that contains less quinidine than Avanir's Neudexta, which could have broader consideration than the approved Neudexta as a result. Today Avanir announced 786 is moving into Phase 2 as an adjunctive treatment for depression, triggering a $2mm milestone to Concert upon dosing. 786 can utilize extensive data generated by Neudexta, a notable efficiency that could help 786 move rapidly into Phase 3 in agitation associated with Alzheimer's disease in 2015, and into other indications as well. Concert could receive $164mm in additional milestones and royalties from the mid-single digit to low double digits on sales of AVP-786.

CTP-354 Recently Gained Some Room to Maneuver From FDA. CTP-354, is a subtype-selective GABA-A modulator, with familiar yet distinctive GABA agonist activity, and a profile of minimal sedation compared to benzodiazepines. FDA recently permitted 354 dosing in humans to be increased, a positive signal for the safety of 354, as it lifted a partial clinical hold due to the submission of additional preclinical data. We believe '354 has the potential for utility not only in spasticity associated with both multiple sclerosis (MS) and spinal cord injury, but we believe there is significant potential for its development in anxiety and pain settings over time. '354 should move into Phase 2 for spasticity in spinal cord injury in 2H14 and into other indications during 2015.

Recent Positive Discussions With FDA for CTP-499. CTP-499, a deuterated-PDE inhibitor for diabetic kidney disease, recently finished up encouraging Phase 2 work, where it demonstrated a reduction in the number of patients progressing toward more serious forms of that condition. After discussions with FDA, Concert is able to conduct a single large trial or two Phase 3 studies utilizing a relatively new endpoint, the reduction of a composite endpoint of increases in serum creatinine (greater than or equal to 50%) or end stage renal disease. In Phase 2, CTP-499 demonstrated a statistically significant reduction in large serum creatinine increases in diabetic kidney disease patients, which bodes well for the molecule for this new endpoint. The company is seeking a SPA for 499, and prefers to partner it for this indication, which we believe can occur during 2015.

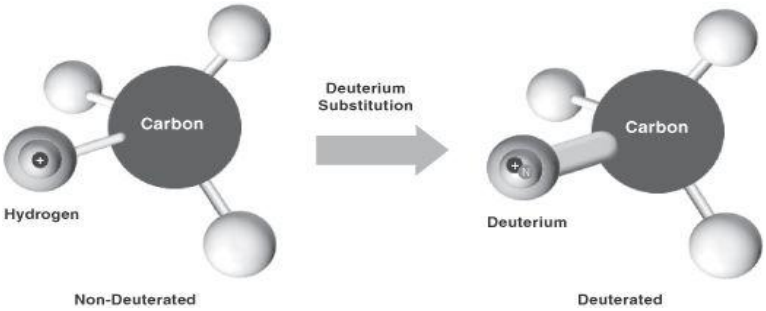
Concert's Other Partnered Programs Have Potential As Well. Jazz Pharmaceutical's JZP-386 is a deuterated analog of sodium oxybate, the active ingredient in Xyrem, a brand which reached revenue of $569mm (+50%) in 2013. JZP-386 has the potential to avoid Xyrem's inconvenient intra-night dosing, and is expected to move into Phase 1 for narcolepsy this year, triggering a milestone. Concert also has a broad-ranging agreement with Celgene for multiple deuterated compounds in inflammation and oncology. These include CTP-730, which is moving into Phase 1 for inflammatory diseases. Though the specific molecules have not yet been disclosed, the Celgene agreement is potentially very lucrative, with $35mm upfront, $1.4B in milestones, and low double-digit royalties.

CNCE Valuation: Attractive In Our View. We value CNCE shares at $24, based on fully-taxed, risk-weighted NPV calculations that totals $24.20. We assess Concert's major assets at the following NPV/CNCE share: CTP-354 at $7.17, CTP-499 at $5.16, and the Avanir, Jazz, and Celgene collaborations at $3.87, $2.37, and $3.61, respectively, with cash and other assets comprising the difference. We continue to rate CNCE shares Buy.

Concert Pharmaceuticals – Executive Summary

Concert Pharmaceuticals: Developing Deuterium-Based Drugs. Founded in 2006, Concert Pharmaceuticals focuses on creating and developing new medicines through its proprietary DCE (deuterated chemical entity) Platform. The DCE Platform selectively employs deuterium, a naturally-occurring relative of hydrogen. Deuterium modification of a molecule has the potential to improve its metabolic properties, with minimal change to its intrinsic pharmacology. Concert's business strategy initially involved establishing novel intellectual property for a number of deuterium-modified molecules across a wide range of therapeutic classes, and then advancing the most promising initial candidates, even as it continued to develop others. Five of these more mature deuterated assets are now currently in active development under the guidance of either Concert or its strategic partners, and all five should be advancing in the clinic by year-end 2014.

Exhibit 1: Deuterium Substitution



Source: Concert Corporate Fact Sheet, May 2013.

The application of deuterium medicinal chemistry to compounds with well understood therapeutic utility can potentially provide an approach with modestly reduced risk with regard to creating new drugs. Concert believes (and we concur) that since its assets are generally materially related to a parent molecule, once Phase 1 is established for the deuterated molecule, especially in an indication that the parent shares, the program has been materially de-risked.

Deuterium Medicinal Chemistry In Brief. Deuterium is one of two naturally-occurring stable isotopes of hydrogen. Where hydrogen has one electron and one proton, deuterium also has a neutron in its nucleus, resulting in an atomic mass that is double that of hydrogen. Deuterium is not radioactive, and possesses physicochemical properties that are similar to those of hydrogen, but because of its increased mass, bonds involving deuterium are generally stronger than similar bonds with hydrogen. This strengthening can be enough to make significant changes in biological reactions with deuterium-based compounds compared to hydrogen-based ones. Many drugs are metabolized by pathways that involve the breakdown of carbon-hydrogen bonds, and the stronger deuterium-based bonds have the potential to alter or deflect the breakdown of the molecule or its metabolites. Deuterium modification therefore offers an approach to potentially creating significantly differentiated new medicines, and importantly, because the behavior of deuterium based bonds is not inherently predictable, novel intellectual property can be established.

Concert's Drug Development Approach. Concert's strategic development of deuterium-based molecules began with management initially broadly examining a host of both approved and novel molecules to selectively apply deuterium and establish intellectual property. Having now established a broad portfolio of deuterated molecules that span multiple therapeutic areas, it continues with that process. We note that

Concert's management team is well-seasoned in therapeutics development, having material experience at Vertex, Merck, Amgen, and other organizations; because of this, we believe Concert should have the ability to successfully navigate the development of its wide range of assets. With existing therapies, Concert is often utilizing significant information regarding the related non-deuterated (parent) compound, allowing it to efficiently identify lead compounds. In some cases, Concert or its partners can truncate the development timeline of a deuterated molecule compared to conventional drug development by sourcing the data from the related parent molecule.

Concert's Pipeline: Five In The Clinic During 2015. Concert has a solid pipeline of deuterated compounds as noted in Exhibit 2. Concert's five most advanced programs are all expected to be materially progressing at various stages in the clinic by the end of 2014. Concert has two proprietary compounds and three partnered programs of significant importance. Given the urgency with which Concert has established its intellectual property, we expect continued advancement of new compounds in its proprietary pipeline into the clinic.

Concert's Proprietary Pipeline: CTP-354 Has A Familiar Yet Distinctive GABA Profile. CTP-354 is Concert's GABA-A selective modulator moving into Phase 2 for spasticity associated with both multiple sclerosis and spinal cord injury. It also could be considered for other much broader indications such as anxiety and neuropathic pain. CTP-354 is attempting to demonstrate efficacy in these settings without the sedation seen with other common GABA-focused therapies, and the larger opportunities such as anxiety and pain with limited sedation gives this compound considerable potential. Phase 2 should begin in 2H14 for the spasticity settings.

Concert's Proprietary Pipeline: CTP-499--Finishing Phase 2 in Diabetic Kidney Disease. CTP-499 is a PDE-inhibitor with anti-inflammatory and anti-fibrotic characteristics that has shown encouraging results in Phase 2 for diabetic kidney disease, and recent changes in trial endpoints have become helpful to the development of therapeutics for this indication. Also, since its parent molecule is pentoxifylline, CTP-499 could have potential for long-term consideration in hepatic settings such as alcoholic liver disease and NASH. '499 could be partnered after the recent positive end-of-Phase 2 meeting with FDA, and the upcoming issuance of a potential SPA for the program.

Exhibit 2: Concert Pharmaceuticals - Pipeline

Product Candidate	Lead Indication(s)	Preclinical	Phase I	Phase 2	Anticipated Milestones	Potential Deal Value	Worldwide Rights
CTP-354	Spasticity associated with MS				▪ Ph1 MAD data expected 2H14 ▪ Ph2 program expected to begin 2H14		CoNCERT Pharmaceuticals Inc.
	Spasticity associated with SCI						
CTP-499	Diabetic Kidney Disease				▪ End of Ph2 FDA meeting expected mid-2014		CoNCERT Pharmaceuticals Inc.
AVP-786 (Deuterated dextromethorphan)	Neurologic and Psychiatric Disorders				▪ Ph2 trial for treatment-resistant major depressive disorder expected to begin 2H14	▪ $170 Million	AVANIR pharmaceuticals
CTP-730	Inflammatory Diseases				▪ Phase 1 expected to begin 2014	▪ $1.4 Billion	Celgene
JZP-386 (Deuterated sodium oxybate)	Narcolepsy				▪ Phase 1 expected to begin 2014	▪ $117 Million	Jazz Pharmaceuticals
C-10068	Pain and Seizures						CoNCERT Pharmaceuticals Inc.
Deuterated ivacaftor	CF and COPD						CoNCERT Pharmaceuticals Inc.

Source: Concert Pharmaceuticals corporate presentation; June 2014.

Partnered Programs With Avanir, Jazz, and Celgene, Are Advancing. Concert initially implemented a partnering strategy for the development of its molecules in order to defer risk, and help establish and validate its DCE platform. It has three corporate agreements so far, and we believe there is the potential for additional collaborations over time. Concert has structured its partnerships with material developmental milestones, providing the company with potential for material cash and revenue generation from those programs even prior to the introduction of its own proprietary therapies.

AVP-786 with Avanir for Neurologic/Psychiatric Disorders. Avanir's (AVNR, $5.33; Not Rated) AVP-786's is a deuterated version of Avanir's approved Neudexta, indicated for pseudobolar affect (sudden, frequent episodes of laughing and/or crying). AVP-786 contains much less quinine than Neudexta, which could make its appeal much broader. '786 is being developed in treatment-resistant depression and neuropathic pain, and is now entering Phase 2 for major depressive disorder. Indications such as agitation in Alzheimer's disease and Parkinson's dyskinesia are also likely. Concert can earn up to $166 million in additional regulatory, development, and sales milestones, and a royalty in the mid-single digits to low double digits on global sales.

Jazz's JZP-386 – A Better Xyrem? Jazz's (JAZZ, $142.04; Not Rated) JZP-386 is a deuterated analog of sodium oxybate that is nearing Phase 1 development for narcolepsy; sodium oxybate is the active ingredient in Jazz's large and rapidly growing Xyrem franchise; Xyrem posted revenue of $569 million in 2013, up +50% from the previous year. JZP-386 has the potential to materially expand the franchise by avoiding the cumbersome middle-of-the-night dosing. Concert can earn up to $117 million in regulatory, development, and sales milestones, and a royalty in the mid-single digits to low double digits on worldwide sales.

Celgene's Inflammation/Oncology Programs. Celgene's (CELG, $84.93; Not Rated) deuterated CTP-730 is in development for inflammatory diseases, and is expected to enter the clinic this year, with Phase 1 results expected in 2015. Though the specific target and parent molecule of CTP-730 has not been disclosed, milestones of up to $1.4 billion point to the deal's significance (the deal also includes three other potential assets). In terms of inflammatory indications and franchises of importance to Celgene, we note that Thalomid has one inflammatory indication, and Celgene's pipeline contains Otezla/apremilast, pomalidomide, CC-220, CC-292, and others that are being examined for inflammatory indications. We expect greater visibility for this collaboration in 2015.

Exhibit 3: Concert – Recent Events/Upcoming Catalysts

Date	Event	Comment	Significance
Feb-12	Avanir deal for deuterated dextromethorphan	Program gives solid PK profile with less quinidine	◆◆◆
Feb-13	Jazz deal for deuterated Xyrem (sodium oxybate)	Extension of significant Xyrem franchise	◆◆◆◆
Apr-13	Celgene collaboration - CTP-730, others	Large deal: $35mm UF, $1.4B MS, SD/low DD royalty	◆◆◆◆◆
Feb-14	Concert IPO	Capital to advance internal programs more rapidly	◆◆◆◆◆
Apr-14	P2 data for CTP-499 in diabetic kidney disease	Showed signal, leading to end of P2 FDA meeting	◆◆◆◆
2H14	Avanir AVP-786 into Phase 2 in treatment res't dep'n	Phase 2 start triggers $2mm milestone to Concert	◆◆◆
2H14	Jazz JZP-386 moves into P1 in narcolepsy	Completion of P1 in 2015 to trigger milestone	◆◆◆
2H14	CTP-354 completes MAD study	Important for '854 in a range of indications	◆◆◆
2H14	CTP-354 FDA discussion about higher doses	Could lead to '854 in pain, other indications	◆◆◆◆
2H14	CTP-354 into Phase 2 in spasticity (spinal)	Data for this indication, should help establish PoC	◆◆◆
2H14	CTP-499 end P2 Meeting w/FDA	Should clarify Phase 3, lead to SPA, pot. partner	◆◆◆◆
2H14	Celgene's CTP-730 to start Phase 1 study	Program progress good visibility for Concert	◆◆◆◆
2015	CTP-354 moves into Phase 2 in spasticity (MS)	Data for this indication, should help establish PoC	◆◆◆
2015	Avanir to move '786 into P3 in Alzheimer's agitation	Phase 3 start triggers $2mm milestone to Concert	◆◆◆◆
2015	Additional Concert proprietary assets progress	Concert's DCE platform should broaden during 2015	◆◆◆◆
2015	Jazz JZP-386 completes P1 in narcolepsy	Completion of P1 triggers $4 milestone	◆◆◆
2015	Celgene's CTP-730 Phase 1 data	Results trigger $8mm milestone, visibility for Concert	◆◆◆◆
2016	CTP-354 Phase 2 data in spasticity (MS, spinal)	Data in the indications could be a major catalyst	◆◆◆◆

(Significance: ◆ least important., ◆◆◆◆◆ most important.)

Source: Ladenburg Thalmann BioPharmaceuticals Research.

Concert Pharmaceuticals – Upcoming Potential Catalyst for 2014, 2015

Concert's Proprietary Programs

- **CTP-354** completed additional preclinical toxicology work, and FDA has recently allowed repeated dosing with the molecule above 6mg. We expect clearance from the agency during mid-2014, providing some room for this drug to be dosed higher, if necessary in the pain indications. '354's top-line receptor occupancy data, important for licensing, should be released mid-year.

- **CTP-354** should also move into phase 2 during 2H14 for spasticity associated with spinal cord injury, and in early 2015 for spasticity associated with multiple sclerosis. Data from these Phase 2 studies should read out during 2016. Other larger opportunities such as anxiety and pain also have the potential to begin during 2015.

- **CTP-499** has shown encouraging results in Phase 2 for diabetic kidney disease, and recent changes in trial endpoints have become helpful to the drug development for this indication. Clarity on Phase 3 trial design, an SPA, and a potential partnership could happen in that order over the next 12 months.

Concert's Partnered Programs

- **Avanir's AVP-786,** a deuterated Neudexta, just entered Phase 2 for treatment resistant major depressive disorders, triggering a $2 million milestone upon dosing initiation. AVP-923 (Neudexta) is now fully enrolled in a Phase 2 study in patients who have material agitation associated with Alzheimer's disease. Avanir has stated repeatedly that it intends to move forward with AVP-786 for the indication, creating the potential for '786 to move into Phase 3 during 2015, with a favorable readout for the Phase 2 study. Movement into additional indications for 786 is possible in 2014/15.

- **Jazz's JZP-386,** a deuterated analog of Xyrem could move into Phase 1 for narcolepsy; When JZP-386 completes a P1 study with this molecule, a $4 million milestone payment is due to Concert. Advancement of this next-gen version of Xyrem, a $500+mm program, should be a catalyst for CNCE shares.

- **Celgene's deuterated CTP-730** is in development for inflammatory diseases, and is expected to enter the clinic this year, with Phase 1 completion expected in 2015, triggering an $8mm milestone. Advancement of this program has the potential to be a material catalyst for CNCE shares, despite not knowing material program specifics at this point.

Concert Pharmaceuticals - Valuation

Concert and CNCE Shares Valuation. Because Concert's operations have the potential for significant revenue and earnings variability over the coming quarters and years, we value the company and its assets using a fully-taxed, risk-weighted net present value methodology for each of its assets. We note that with its multiple partnerships and advancing clinical programs, Concert has a diverse portfolio of therapeutic assets, and we assess the total value of these programs at $24.20 per CNCE share, which underpins our $24 CNCE price target (see Exhibit 4).

Valuing Concert's Proprietary Pipeline. Concert's two most advanced proprietary assets, CTP-354 for spasticity, and CTP-499 for diabetic kidney disease, have material valuation potential, in our view. CTP-354 for spasticity as a result of multiple sclerosis

and/or spinal cord injury and possibly other indications such as anxiety and neuropathic pain, is moving into Phase 2. We believe that a GABA-A modulator with familiar GABA mechanism, yet a distinct profile, with once-daily dosing and less sedation, should have material potential for consideration in spasticity, anxiety, and even pain settings, and have the potential to exceed $1 billion in peak revenue. We value its collective opportunities at $7.17 per share. CTP-499, for diabetic kidney disease appears to have achieved material validation after a more full analysis of its Phase 2 trial data, which bodes well for Phase 3 consideration. We assume licensing is to occur after discussions with FDA now that Phase 2 is winding up. Despite risks to the Phase 3 endpoints that remain, we believe more reasonable guidance is emerging along those lines from FDA, and estimate CTP-499 at $1 billion peak revenue, and value the program at $5.16 per CNCE share. Other less mature proprietary products are much more modest opportunities at this point and valued at $0.31 per CNCE share, though proof of concept comes at Phase 1 for many of these deuterated programs, and this part of the portfolio could appreciate quite quickly.

Exhibit 4: Concert – CNCE Share NPV Summary ($000, except per share amts)

Concert Pharmaceuticals - Assets	NPValue	NPV/Share
CTP-354 - Spasticity, Anxiety, others	$ 128,386	$7.17
CTP-499 - Diabetic Kidney Disease	$ 92,330	$5.16
Other Proprietary Dueterated Assets	$ 5,468	$0.31
AVP-786 - CNS indications (Avanir)	$ 69,267	$3.87
JZP-386 - Sleep indications (Jazz)	$ 42,464	$2.37
CTP-730 - Inflammation (Celgene)	$ 54,214	$3.03
Other Celgene - Onc/Inflam (Celgene)	$ 10,421	$0.58
Other Corporate	$ (74,354)	($4.15)
Net Cash	$ 95,006	$5.31
NOLs, Credits, etc.	$ 10,052	$0.56
Concert - Company Valuation	**$ 433,253**	**$24.20**

Source: Ladenburg Thalmann BioPharmaceuticals Research.

Valuing Concert's Collaborations. Regarding Concert's partnered portfolio, Avanir seems to be operating with a good urgency with AVP-786, and is exploring dextromethorphan's broad neurotransmitter receptor activity with the molecule, looking at the therapy in multiple additional indications in addition to depression, including agitation and dyskinesia. Because of these multiple indications, and its potential for its rapid advancement, the economics of this program are valued at $3.87 per CNCE share. The Jazz program JZP-386 attempts to provide the Xyrem franchise with a product that doesn't have middle of the night dosing, and can help protect against potential loss of exclusivity. Xyrem is growing rapidly (+50% yr/yr) and is large at $569 million in 2013, and making a more convenient dosing form with longer patent life appears to be a material opportunity, generating a $2.37 NPV per CNCE share. Finally Celgene has not disclosed the mechanism of CTP-730 inflammation collaboration, though the very large regulatory milestones and peak revenue along the lines of Xyrem, give this collaboration a $3.03 NPV, by our calculation. The remainder of the Celgene assets are estimated at $0.58, and net cash, NOLs and the drag of general corporate expense totals $1.72 per CNCE share, yielding the $24.20 total, driving our $24 CNCE shares price target.

Concert Pharmaceuticals – In Depth

Deuterium Medicinal Chemistry - In Brief

Deuterium – Fast Facts. Deuterium is one of two naturally-occurring stable isotopes of hydrogen. The far more common hydrogen isotope, protium, has no neutron in its nucleus. Deuterium, however, has a nucleus that contains both one proton and one

neutron. Deuterium's symbol is D or ^{2}H. Deuterium possesses physicochemical properties that are similar to those of hydrogen, but its atomic mass is double that of hydrogen due to the presence of the additional neutron. Deuterium has a presence in the ocean water of about 0.0156% per each hydrogen atom, and is generally produced by starting with water, which contains a small amount of heavy water, where deuterium replaces the hydrogen in the water molecules; this heavy water is then separated for the deuterium. According to Concert (and multiple other sources), the average human body contains about 2 grams of deuterium.

Deuteration – General Effects on a Molecule. Chemically, deuterium behaves comparably to ordinary hydrogen, but there are differences in bond energy and bond length for compounds that are deuterated isotopes; these differences are larger than the isotopic differences in any other element. Bonds involving deuterium (and another more rare hydrogen isotope, tritium) are somewhat stronger than the corresponding bonds in hydrogen, enough to occasionally create significant changes in biological reactions. This is because many drugs are metabolized by pathways that involve the breaking of carbon-hydrogen bonds, and having stronger deuterium-carbon bonds or bonds helps deflect or prevent the breakdown of the bonds. Incorporation of deuterium in place of hydrogen at selective points in the molecule therefore has the potential of retaining the biochemical potency and selectivity of a physiologically active compound, while potentially modifying its metabolic properties, and substantially altering its therapeutic profile.

Deuteration in Drug Development: Material Advancements, Fresh IP. Deuterated compounds have been used in the clinic for some time as probes for pharmacokinetic and metabolism studies of the related non-deuterated therapeutics, though only relatively recently has deuterium modification received attention as an approach to creating enhanced therapeutics—Concert Pharmaceuticals is a leader in this field of medicinal chemistry. Deuteration can enhance bioavailability and improve the half-life of a compound, and deuterium substitution at specific molecular positions can improve metabolic stability, reduce or eliminate the formation of toxic metabolites, or even increase the formation of desired active metabolites. However, when deuterium is incorporated at a known site of oxidative metabolism, because of the complexity of the process, deuterium's effects on the absorption, distribution, metabolism, and excretion of a molecule is inherently unpredictable. For example, complex enzymatic metabolism may often have other rate-limiting steps, and/or the presence of a stabilized carbon-deuterium bond may cause metabolism to shift to another site or sites on the molecule. Since the behavior of the deuteration of a molecule is largely unpredictable (non-obvious), deuterated compounds are therefore able to generate new intellectual property.

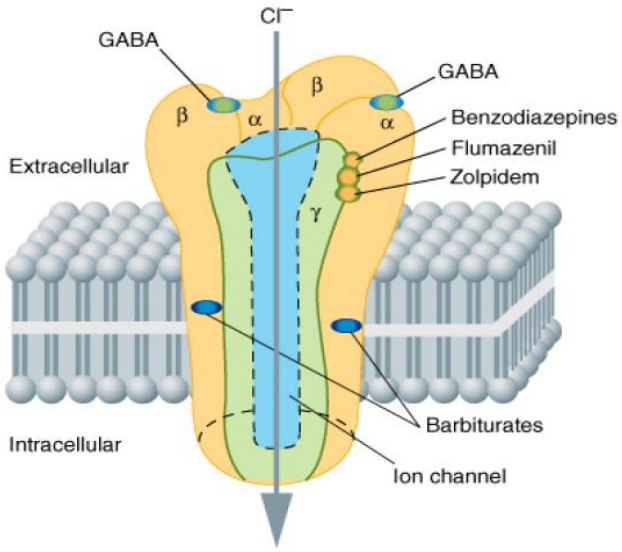
Deuteration May Result In A Truncated Development Scheme. The application of deuterium to a molecule has the potential, depending upon specifics of the program, to have some elements of its development program truncated/reduced. For instance, with the Avanir program, FDA has permitted Avanir to utilize data generated from its dextromethorphan-based program (in this case, a different asset called AVP-923) and apply it to the development package for the deuterated dextromethorphan analog AVP-786 that Avanir licensed from Concert. This should help '786 without duplicating the entire clinical program of '923, but it can instead be substituted when the POC in a particular indication has been established. It is uncertain if this type of consideration is possible for all programs, though when it is, it should be clearly beneficial in terms of development time, spending, and efficiencies.

Concert Pharmaceuticals - Proprietary Programs in the Clinic

CTP-354 – A Non-Sedating GABA Modulator for Spasticity, Anxiety, and Pain

GABA-A Receptor Background. GABA is the major inhibitory neurotransmitter in the nervous system, and has been well characterized and studied over several decades. (Its stimulatory counterpart is glutamate.) The GABA-A receptor is a well-characterized, ionotropic receptor that is activated by GABA, and is the target of multiple well validated therapeutics, such as the benzodiazepines (e.g., Valium, Xanax, and others). Indications for therapeutics targeting this receptor include anxiety, insomnia, and spasticity, among others. The GABA-A receptor is a pentameric protein with subtypes composed of α, β, and γ subunits (Exhibit 5). The active site of the GABA-A receptor is the binding site for GABA and for several therapeutics as well. The GABA-A receptor also contains a number of allosteric binding sites that modulate the activity of the receptor indirectly.

Exhibit 5: The GABA-A Receptor and Therapeutic Binding Sites



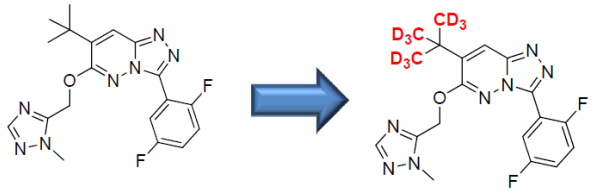
Source: Katzung BG, Masters SB, Trevor AJ: Basic & Clinical Pharmacology, 11th Edition.

GABA-A Activation. Typical benzodiazepines such as Valium, Xanax, and others, activate the GABA-A receptor in a non-selective manner by binding to an allosteric site at the interface of a γ subunit and either an α1, α2, α3, or α5 subunit. Benzodiazepines are well known for their efficacy in anxiety, spasticity, and insomnia, though their use is limited due to poor tolerance, sedation, and drug interactions, some of which is believed to occur due to a relative lack of GABA-A subtype selectivity. Preclinical work indicates that the sedative, ataxic, and dependence effects of benzodiazepines are mediated by the α1 subtype (sleep drugs such as Ambien activate the α1 subunit). Agonism at the α2 and α3 subtypes is believed to be associated with anxiolytic, analgesic, and spasmolytic activities, whereas α5 subtype activity is believed to have cognitive effects.

CTP-354 Development. CTP-354 is a subtype-selective GABA-A modulator, and Concert is developing it for use in spasticity, neuropathic pain, and anxiety disorders. CTP-354 is an analog of L-838417, a compound that was developed as part of Merck's research effort towards subtype-selective GABA-A anxiolytics that could potentially have reduced sedation and ataxia. The Merck (MRK, $58.86; Not Rated) compound was selected due to its promising pharmacology: L-838417 demonstrated an attractive

subtype-selective GABA-A profile, with partial agonism at α2, α3, and α5 subtypes, and antagonism at α1. L-838417 has been reported to be efficacious in preclinical models of inflammatory and neuropathic pain, in addition to having anxiolytic activity and strong muscle relaxant effects. However L-838417 possessed a poor preclinical pharmacokinetic profile, and despite considerable preclinical work, was not advanced materially into the clinic.

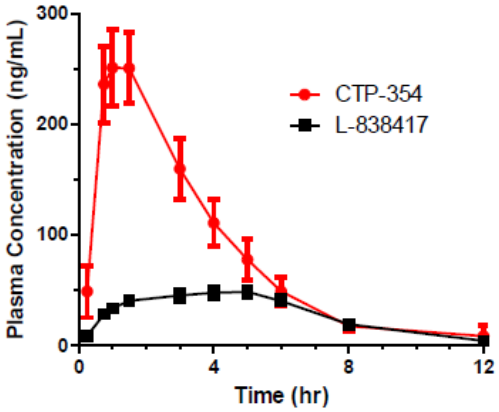
Exhibit 6: CTP-354 (C-21191) – A Deuterated GABA-A Modulator



Source: Liu, et al. C-21191: Deuterated Subtype-Selective GABA-A Modulator for Spasticity and Neuropathic Pain, Neuroscience 2011.

Concert deuterated L-838417 as mentioned above, by incorporating nine deuterium atoms in place of hydrogen at key positions to overcome its poor pharmacokinetics (Exhibit 6), thus creating CTP-354 (formerly known as C-21191). With Concert's selective incorporation of deuterium, the pharmacokinetics of CTP-354 has been dramatically improved (Exhibit 7). Concert moved CTP-354 into the clinic and is developing it in multiple attractive indications.

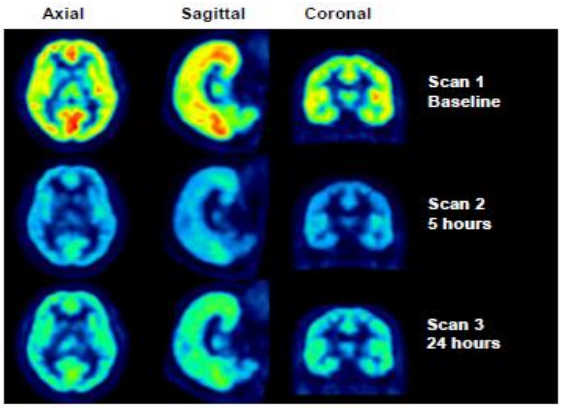
Exhibit 7: Improved PK of Deuterated CTP-354 vs. L-838417 (Rat data)



Source: Liu, et al. C-21191: Deuterated Subtype-Selective GABAA Modulator for Spasticity and Neuropathic Pain, Neuroscience 2011.

'354 Retains Selective GABA-A Pharmacology. Importantly, deuterium substitution does not change the intrinsic pharmacology of CTP-354: Both L-838417 and CTP-354 have demonstrated binding to the benzodiazepine site of the GABA receptor with no significant off target activities. Specifically, CTP-354 has been shown to lack agonist activity at the GABA-A α1–receptor subtype, which should confer a lack of sedation with the compound, but it also has potent partial agonist activity at other key GABA-A receptor subtypes that was noted with L-838417. CTP-354's broader profile is shaping up well, as it has shown no apparent sedation at therapeutic doses.

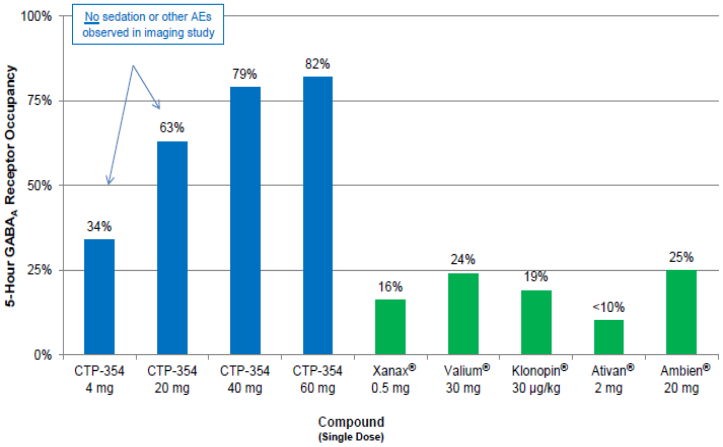
Exhibit 8: CTP-354 Brain Receptor Occupancy



Source: Concert Pharmaceuticals corporate presentation May 2014.

CTP-354 Clinical Development Appears Promising. Concert has moved CTP-354 into the clinic, where it has shown promise. The single ascending dose (SAD) studies have demonstrated a long plasma half-life, consistent with once-daily dosing, with no serious adverse events. The molecule has sustained high brain receptor occupancy (Exhibit 8), a key characteristic for these compounds. Importantly, CTP-354 appears less sedating at higher GABA-A receptor occupancy levels than benzodiazepines (Exhibit 9); no sedation, ataxia, or adverse effects have been observed with a single 20mg dose that yields 60% receptor occupancy at 24 hours. Concert has modeled that the 6mg dose should achieve this level of receptor occupancy.

Exhibit 9: CTP-354: Less Sedating At Higher Receptor Occupancy Than BZDs



Source: Concert Pharmaceuticals corporate presentation May 2014.

CTP-354 Clinical Considerations: Doses Above 6mg To Be Considered Over Time. Phase 1 results in a single ascending dose trial in 71 healthy volunteers in doses ranging from 0.15mg to 60mg show that a maximum tolerated dose was not reached, despite receptor occupancy saturation. The long plasma half life supports once-daily dosing, and a multiple ascending dose trial is underway, which should enroll up to 62 healthy volunteers. Dosing was from 2mg to 6mg over 10 days, and due to a partial clinical hold, dosing is limited to 6mg for now—no specific adverse event was seen, but due to a lack

of MTD, Concert was limited to 6mg in MAD and 60mg in SAD studies. Concert has conducting studies designed to permit increased doses, which FDA permitted in July 2014. Phase 2 trials in the spasticity indication are to begin in 2H14, and they could progress fairly rapidly. In summary, with a profile demonstrating low sedation, combined with activity not only in spasticity, but in anxiety and neuropathic pain settings, we believe the competitive positioning of CTP-354 is shaping up to be quite promising.

Spasticity Description/Background. Spasticity is characterized by involuntary muscle spasm; it can result from a wide range of disorders, including multiple sclerosis (MS), spinal cord injury, cerebral palsy, amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), stroke, and hereditary spastic paraplegia. Symptoms can range from mild muscle tightness to more severe symptoms, including the painful inability to move limbs that can result in disability and diminished quality of life. The American Association of Neurological Surgeons estimated in 2006 that there were 12 million patients suffering from spasticity, including about 80% of people with MS. Of the estimated 400,000 patients with MS in the US, Concert estimates that at least 34% (140,000 patients), suffer from moderate to severe spasticity. Regarding spasticity associated with spinal cord injury, approximately 270,000 people in the US suffer from that condition (with 12,000 new incidences annually) according to Concert. 65% to 78% of those spinal cord injury patients experience some degree of spasticity, and Concert estimates that 28% to 46% of those (80,000 to 120,000 patients) suffer from problematic spasticity and could be candidates for therapy (Exhibit 10).

Exhibit 10: CTP-354 Initial Spasticity Target Markets

	US Disease Prevalence	% Treatable Spasticity*	Treatable Population
MS	400,000	34+%	140,000
SCI	270,000	28-46%	80,000–120,000

Source: Concert Pharmaceuticals corporate presentation March 2014.

Treatment of spasticity is through exercise, physical therapy, pharmacologic therapy, or surgery. Pharmacologic therapies considered include: baclofen (Lioresal) a GABA-B agonist, and tizanidine (Zanaflex) an $\alpha 2$ adrenergic agonist. Drowsiness and sedation are seen with both, and hypotension and multiple drug/drug interactions are seen with Zanaflex. Other therapeutics that may be considered include botulinum toxin (Botox) which is injected into the affected muscles, and a cannabis extract containing dronabinol and cannabidiol (Sativex) is also under development for spasticity associated with MS and is approved in the EU.

CTP-354 Economics in Spasticity, Anxiety, and Other Indications. With regard to CTP-354's use in spasticity, due to the familiarity with the GABA-A receptor-related mechanism, and the compound's potential once-daily profile, we assume a peak penetration of one-third of the addressable market for both MS and spinal cord injury, or just over 79,000 patients treated at peak in the US. We assume $5,000 per patient per year at peak, resulting in peak revenue for CTP-354 of $400 million in the US for this indication. For EU/international revenue, we assume slightly greater patient numbers, though lower pricing, and arrive at roughly the same figures. We model a partner for international rights with Concert garnering $20 million upfront, $150 million in milestones, and 15% to 25% royalties on international sales, to be signed post-Phase 2 data. We assume a 2019 launch, and also assume additional indications for anxiety, a natural, since the BDZs are widely considered there, and in various pain settings where '354 has shown activity.

Exhibit 11: CTP-354 – NPV Calculation to Concert (2014 – 2030)

	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
CTP-354 - Spasticity, Anxiety	-	-	-	-	-	**35,000**	**250,000**	**450,000**	**700,000**	**975,000**	**1,225,000**	**1,425,000**	**1,675,000**	**1,875,000**	**2,125,000**	**2,225,000**	**2,325,000**
US Sales	-	-	-	-	-	25,000	175,000	275,000	425,000	600,000	750,000	850,000	1,000,000	1,100,000	1,250,000	1,250,000	1,250,000
Int'l Sales	-	-	-	-	-	10,000	75,000	175,000	275,000	375,000	475,000	575,000	675,000	775,000	875,000	975,000	1,075,000
Intl Royalty Rate (15%-25%)	-	*0%*	*0%*	*0%*	*0%*	*15%*	*15%*	*15%*	*15%*	*20%*	*20%*	*20%*	*25%*	*25%*	*25%*	*25%*	*25%*
Intl Royalty	-	-	-	-	-	1,500	11,250	26,250	41,250	75,000	95,000	115,000	168,750	193,750	218,750	243,750	268,750
Upfront/Milestones	-	-	20,000	10,000	10,000	50,000	-	-	-	-	-	25,000	-	-	-	-	100,000
Total Revenue to Concert	-	-	20,000	10,000	10,000	76,500	186,250	301,250	466,250	675,000	845,000	990,000	1,168,750	1,293,750	1,468,750	1,493,750	1,618,750
Concert Expenses																	
COGS (US only)	-	-	-	-	-	1,250	8,750	13,750	21,250	30,000	37,500	42,500	50,000	55,000	62,500	62,500	62,500
COGS pct	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
SG&A	-	-	-	1,000	2,500	40,000	55,000	60,000	65,000	70,000	80,000	80,000	85,000	85,000	85,000	90,000	95,000
R&D	5000	10,000	12,000	12,000	12,500	12,500	10,000	10,000	10,000	10,000	5,000	5,000	-	-	-	-	-
Total Expense	5,000	10,000	12,000	13,000	15,000	53,750	73,750	83,750	96,250	110,000	122,500	127,500	135,000	140,000	147,500	152,500	157,500
Net to Concert	**(5,000)**	**(10,000)**	**8,000**	**(3,000)**	**(5,000)**	**22,750**	**112,500**	**217,500**	**370,000**	**565,000**	**722,500**	**862,500**	**1,033,750**	**1,153,750**	**1,321,250**	**1,341,250**	**1,461,250**
NPV/year	-4952.4	-7555.3	4646.1	-1340.2	-1718.2	4129.8	14573.9	20125.8	24455.0	26673.9	24341.5	20755.9	17769.3	14165.7	11576.6	8394.2	6532.3
Discount Rate	15%	30%	30%	30%	30%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
Tax rate used	0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
NPV Taxed (effective rate)	$ (4,952)	$ (7,555)	$ 4,646	$ (1,340)	$ (1,718)	$ 4,130	$ 14,574	$ 13,082	$ 15,896	$ 17,338	$ 15,822	$ 13,491	$ 11,550	$ 9,208	$ 7,525	$ 5,456	$ 4,246

Total Value	**$193,325**
NPV Per Share	**$10.80**
Total Value taxed	**$ 128,386**
NPV/share taxed	**$7.17**

Source: Ladenburg Thalmann BioPharmaceuticals Research.

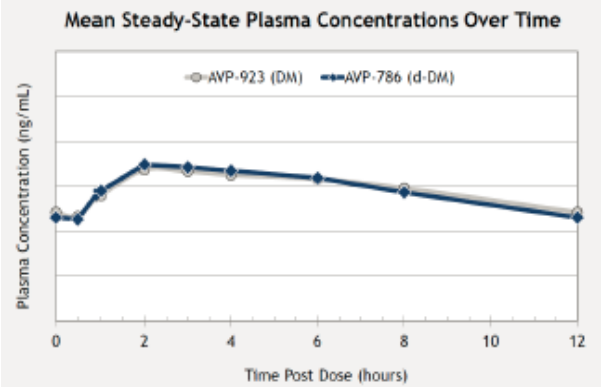
CTP-354: Material Potential. With a familiar yet distinct GABA-A mechanism, and broad activity in multiple settings, and the additional larger indications adding over $1 billion in total revenue at peak, we estimate that collectively these indications provide the molecule with revenue totals in excess of $2 billion. Given that some safety work that still needs to be accomplished, despite the well-validated GABA-A receptor mechanism, we assign a relatively high discount of 40% per annum. Taken together, we estimate the fully-taxed, risk weighted economics of CTP-354 to Concert at $7.17 per CNCE share (Exhibit 11). We note that as Concert ticks off the development items, and '354's risk profile is reduced, the potential for a material increase in this program's NPV to Concert exists.

Concert's Avanir Partnership – AVP-786, A Deuterated Neudexta

Neudexta: Potential for Deuterium Improvement. In October 2010, FDA approved Avanir Pharmaceutical's Neudexta (AVP-923), a proprietary combination of dextromethorphan and quinidine, for the treatment of pseudobulbar affect (PBA). Avanir launched the drug in February 2011, and as of March 2014, the brand is annualizing at approximately $100 million in revenue. Neudexta consists of dextromethorphan, an NMDA receptor antagonist and sigma-1 agonist, and the enzyme inhibitor quinidine, a CYP450 2D6 inhibitor, which serves to increase the bioavailability of dextromethorphan. Pseudobulbar affect (PBA) occurs secondary to a variety of neurological conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying; its episodes occur out of proportion to the person's emotional state.

Avanir Deal Background. In February 2012, Concert inked a license agreement with Avanir for worldwide rights to develop and commercialize Concert's deuterated dextromethorphan, now known as AVP-786 (or D-DM). The agreement includes the rights to multiple D-DM compounds, and Avanir has overall responsibility for research, development and commercialization of AVP-786. AVP-786 includes one of the D-DM analogs licensed to Avanir, and is a combination of a deuterium-substituted dextromethorphan analog and an ultra-low dose of quinidine. The deuteration results in a similar pharmacokinetics for Neudexta and AVP-786 (Exhibit 12), yet allows for an ultra low-dose of quinidine to be included in AVP-786, reducing chances for a patient to experience QTc prolongation, and other unpleasant GI adverse events associated with the quinidine.

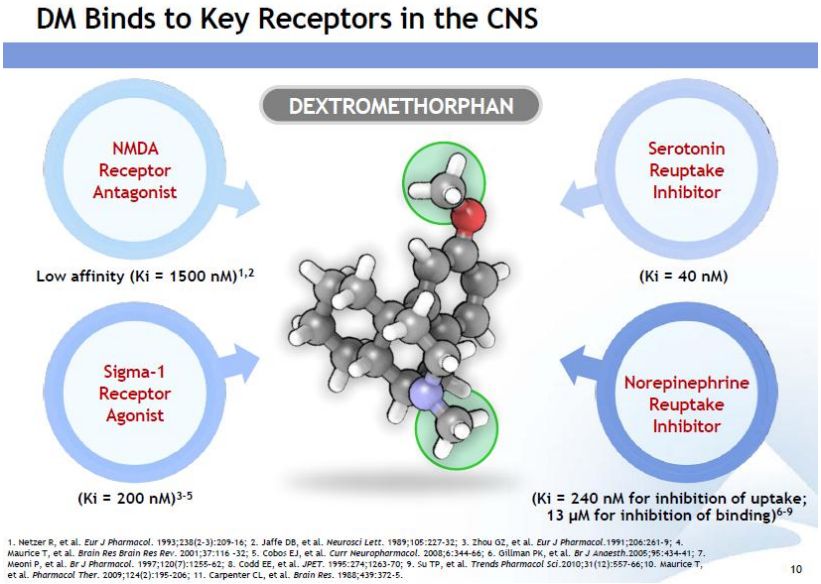
Exhibit 12: AVP-786 Has Similar Pharmacokinetics Compared to AVP-723



Source: Concert Pharmaceuticals corporate presentation Feb 2014

AVP-786 and AVP-923: Truncated Development Timelines. Dextromethorphan acts on sigma-1 and NMDA receptors and is an inhibitor of serotonin and norepinephrine (Exhibit 16). With AVP-786, incorporation of deuterium into specific positions of the dextromethorphan molecule strengthens the chemical bonds and reduces susceptibility to enzyme cleavage and first pass metabolism without altering dextromethorphan's pharmacology, according to Avanir. In addition, it should be noted that Avanir is enrolling patients in a Phase II trial to investigate the use of AVP-923 for the treatment of levodopa induced dyskinesia (LID) in patients with Parkinson's disease (PD), and Avanir was able to gain FDA acceptance that it may apply results from this AVP-923 study (and others) to the AVP-786 program, potentially significantly truncating AVP-786's development timeline in multiple indications.

Exhibit 13: Dextromethorphan: Multiple Receptor Activity in the CNS



Source: Avanir Corporate presentation, May 2014.

Dextromethorphan: Multiple Receptor Activity, Multiple Indications for '786. With broad activity of dextromethorphan on multiple key CNS receptors such as NMDA, serotonin, norepinepherine, and sigma-1, Avanir is developing AVP-786 for the treatment of multiple neurologic and psychiatric disorders. In October 2013, Avanir reported plans to

advance AVP-786 into a Phase 2 trial in the 2H14 for treatment-resistant major depressive disorder in patients with insufficient response to conventional anti-depressants, based on data generated by AVP-923 in patients with PBA and depression noted in Exhibit 14. Moving AVP-786 into Phase 2 triggers a milestone of $2 million to Concert. Other additional indications under consideration either directly with AVP-786 or AVP-923, which will be switched to AVP-786 over time, include agitation in Alzheimer's disease, which has just finished enrollment in Phase 2 (and could move into phase 3 during 2015), neuropathic pain, levodopa induced dyskinesia (LID) in patients with Parkinson's disease (PD), in addition to others that are under consideration in investigator-sponsored trials.

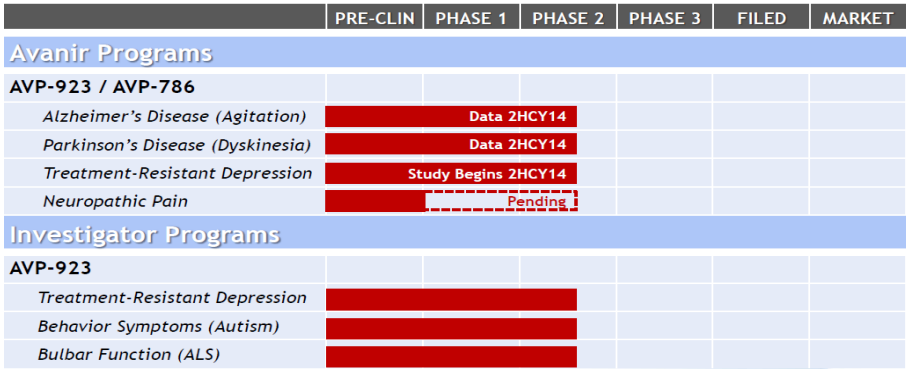
Exhibit 14: Avanir's AVP-923 in Depression in Pseudobulbar Affect Patients

Endpoint	AVP-923 30/10	AVP-923 20/10	Placebo	P Value (30/10 vs. Placebo) (20/10 vs. Placebo)
	(n=50)	(n=55)	(n=52)	
BDI-II	-3.36	-2.3	-1.1	0.065 0.378

Source: Avanir Corporate presentation, March 2014.

Avanir Deal Economics to Concert. Concert received a $2 million upfront payment for the initial deal, and during 2013 it also recognized a $2 million milestone payment based on positive data from Avanir's Phase 1 clinical trial of AVP-786. Concert is eligible to earn up to $4 million in development milestones, up to $37 million in regulatory milestones and up to $125 million in sales milestones. Concert should receive is $2 million for initiation of dosing in a Phase 2 for AVP-786, which should occur imminently as Avanir begins the Phase 2 study in major depressive disorder. Concert is also to receive royalties ranging from the mid-single digits to low double digits on worldwide net product sales, which extends to the longer of specified patent expiration or 10 years following commercial launch. As AVP-786 appears key to Avanir's long-term plans and potential success, we expect a continued rollout of news flow on the various indications being pursued (Exhibit 15). We note positive events for AVP-923 should also be positive for AVP-786 and for Concert.

Exhibit 15: Big Plans for AVP-786 & AVP-923: Both Beneficial to Concert



Source: Avanir Corporate presentation, May 2014.

AVP-786 Opportunity/Economics to Concert. The reduction of quinidine in AVP-786 may free the dextromethorphan asset to be developed in many settings, and Avanir is doing just that, with plans to examine the Concert drug in treatment-resistant depression and neuropathic pain settings (Exhibit 15), among others. All this development should ultimately be beneficial to Concert, as the royalties and milestones accrue. There is also ongoing work with AVP-923 that should benefit AVP-786 as well, in multiple other settings, including agitation in Alzheimer's, Parkinson's dyskinesia, among others. Collectively, success in these indications should also accrue over to AVP-786, so we model its peak

revenue in excess of $1 billion. All in, with revenue and milestones noted above, we estimate AVP-736's fully taxed, risk weighted NPV is $3.87 per CNCE share to Concert (Exhibit 16).

Exhibit 16: AVP-786 NPV Calculation to Concert

	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Avanir - AVP-786	-	-	-	-	-	**67,500**	**170,000**	**295,000**	**430,000**	**565,000**	**692,500**	**820,000**	**947,500**	**1,060,000**	**1,165,000**	**1,270,000**	**1,375,000**
US Sales	-	-	-	-	-	40,000	105,000	170,000	235,000	300,000	365,000	430,000	495,000	560,000	625,000	690,000	755,000
Int'l Sales	-	-	-	-	-	27,500	65,000	125,000	195,000	265,000	327,500	390,000	452,500	500,000	540,000	580,000	620,000
Royalty Rate	-	-	-	-	*5%*	*5%*	*5%*	*7.5%*	*7.5%*	*7.5%*	*10%*	*10%*	*10%*	*12%*	*12%*	*12%*	*12%*
Royalty	-	-	-	-	-	3,375	8,500	22,125	32,250	42,375	69,250	82,000	94,750	127,200	139,800	152,400	165,000
Milestones	2,000	2,000	-	-	10,000	27,000	-	10,000	-	-	50,000	-	-	-	-	65,000	-
Total Revenue to Concert	2,000	2,000	-	-	10,000	30,375	8,500	32,125	32,250	42,375	119,250	82,000	94,750	127,200	139,800	217,400	165,000
Net to Concert	**2,000**	**2,000**	**-**	**-**	**10,000**	**30,375**	**8,500**	**32,125**	**32,250**	**42,375**	**119,250**	**82,000**	**94,750**	**127,200**	**139,800**	**217,400**	**165,000**
Days to End	25.0	390.0	756.0	1121.0	1486.0	1851.0	2217.0	2582.0	2947.0	3312.0	3678.0	4043.0	4408.0	4773.0	5139.0	5504.0	5869.0
Years to end	0.1	1.1	2.1	3.1	4.1	5.1	6.1	7.1	8.1	9.1	10.1	11.1	12.1	13.1	14.1	15.1	16.1
NPV/year	1980.9	1646.0	0.0	0.0	4031.4	9796.3	2191.7	6626.8	5322.1	5594.4	12587.1	6924.2	6400.7	6874.2	6040.4	7514.7	4562.7
Discount Rate	15%	20%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Tax rate used	0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
NPV Taxed (effective rate)	$ 1,981	$ 1,646	$ -	$ -	$ 4,031	$ 9,796	$ 2,192	$ 4,307	$ 3,459	$ 3,636	$ 8,182	$ 4,501	$ 4,160	$ 4,468	$ 3,926	$ 4,885	$ 2,966

Total Value	**$95,987**
NPV Per Share	**$5.36**
Total Value taxed	**$69,267**
NPV/share taxed	**$3.87**

Source: Ladenburg Thalmann BioPharmaceuticals Research.

Concert Pharmaceuticals - Risks

The following Risks include, but are not limited to:

Regulatory/FDA. As with any company whose main business focuses on the development of pharmaceuticals, Concert is subject to the strenuous regulatory requirements of the US Food and Drug Administration (FDA) and other international regulatory agencies such as the EMEA to have its new drugs approved. Promotion of its approved drug products is also highly regulated by FDA and related agencies throughout the globe. Also, in general, though the company's specific focus on ethical (prescription) pharmaceuticals places significant risk on its operations due to the scrutiny of FDA and other governmental regulatory bodies, we believe this specific risk over time should be no greater than that for any other research-based drug development company.

Material Dependence Upon CTP-499, CTP-354 Progress. CTP-354 and CTP-499 are two of Concert's most advanced proprietary clinical candidates in development . These novel molecules may take material time and resources to finish clinical development, if they are able to complete at all, and there is certainly no guarantee that the company will be successful in doing so. In addition, Concert may seek one or more collaborators for future development of CTP-499. There is a risk that the company may not be able to enter into a collaboration for the therapy, or is able to enter into one with terms that are beneficial to CNCE shareholders. These development programs have garnered major investor interest within Concert's operations; if they do not progress, there is material risk that CNCE shares could trade downward.

Risks With Partnered Programs. Concert has a number of partnered programs, including material efforts with Celgene, Jazz Pharmaceuticals, and Avanir Pharmaceuticals. These partnered development programs have garnered major investor interest within Concert's operations. Because these programs are ultimately under the direction of other companies, there is no guarantee those programs will progress at all, or in a way that is beneficial to Concert or CNCE shareholders. If any or all of these programs do not progress in a way that is beneficial to Concert, it is possible that CNCE shares may come under material negative pressure.

Deuteration: Approval, Manufacturing Risks. To the best of our knowledge, no deuterated drug has ever been successfully approved or commercialized. There may be specific risks to gaining licensure for these types of agents from regulatory authorities, though these do not appear to have not emerged at this point. In addition, the company may also incur unforeseen manufacturing challenges with deuterated compounds, or manufacturing costs that are required for the production of any product candidate that receives marketing approval may turn out to be substantial, though excessive cost have not specifically manifested at this point.

Other Risks. Concert has incurred significant losses since inception, expects to incur losses for at least the next several years, and may never sustain profitability. Concert also has a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for future viability. It is an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make its common stock less attractive to investors.

Concert Pharmaceuticals, Inc.	**2011A**	**2012A**	**2013A**	*1Q14A*	*2Q14E*	*3Q14E*	*4Q14E*	**2014e**	**2015E**	**2016E**	**2017E**	**2018E**
Income Statement ($000, except per share amts.)												
Product Revenue												
CTP-354 Total (int'l to partner)	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
CTP-499 Total (top line to partner)	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
Other/Collab revenue	*0*	*0*	*0*	0	0	0	0	*0*	0	0	$ -	$ -
Total Proprietary Sales Revenue	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Milestone & Royalty Revenue												
Total Royalties from Partners	**0**	**0**	**0**	**-**	**-**	**-**	**-**	**0**	**-**	**-**	**-**	**-**
Upfront, Milestones from Partners	$ 5,500	$ 1,500	$ 2,000	$ -	$ -	$ -	$ 2,000	$ 2,000	$ 19,000	$ 13,750	$ 40,750	$ 152,750
License and Development Revenue	**13,967**	**11,349**	**23,408**	**1,613**	**2,000**	**2,250**	**2,500**	$ 8,363	**8,500**	**8,500**	**9,000**	**9,000**
Total Concert Revenue	**$19,467**	**$12,849**	**$25,408**	**$1,613**	**$2,000**	**$2,250**	**$4,500**	**$10,363**	**$27,500**	**$22,250**	**$49,750**	**$161,750**
Expenses:												
COGS	$0	$0	$0	*$0*	*$0*	*$0*	*$0*	$0	$0	$0	$0	$0
R & D	23,436	24,193	21,790	*5,594*	*6,000*	*6,500*	*6,750*	$ 24,844	26,500	30,000	30,000	35,000
S G & A	7,377	7,266	8,028	*2,538*	*2,400*	*2,500*	*2,600*	$ 10,038	10,000	10,200	13,000	20,000
Total Expenses	$30,813	31,459	29,818	$8,132	$8,400	$9,000	$9,350	$ 34,882	$36,500	$40,200	$43,000	$55,000
Operating Income	(11,346)	(18,610)	(4,410)	(6,519)	(6,400)	(6,750)	(4,850)	$ (24,519)	(9,000)	(17,950)	6,750	106,750
Operating Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Interest Income	44	22	20	4	60	65	60	$ 189	150	175	200	800
Interest Expense	(18)	(1,856)	(1,666)	0	0	0	0	$ -	0	(200)	(200)	(200)
Other Income (Expense)	0	0	0	0	0	0	0	$ -	0	0	0	0
Other financing income (expense)	0	0	0	(435)	(100)	(100)	(100)	$ (735)	(500)	(400)	(350)	0
Total Other Income, net	26	(1,834)	(1,646)	(431)	(40)	(35)	(40)	(546)	(350)	(425)	(350)	600
Pretax Income	(11,320)	(20,444)	(6,056)	(6,950)	(6,440)	(6,785)	(4,890)	$ (25,065)	(9,350)	(18,375)	6,400	107,350
Pretax Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Effective Taxes	-	-	-	-	-	-	-	-	-	-	448	9,125
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	0.0%	*0.0%*	*0.0%*	*7.0%*	*8.5%*
Fully Taxed rate	(4,302)	(7,769)	(2,301)	(2,641)	(2,447)	(2,578)	(1,858)	$ (9,525)	(3,553)	(6,983)	2,432	40,793
Tax Rate	*38.0%*	*38.0%*	*38.0%*	*38.0%*	*38.0%*	*38.0%*	*38.0%*	38.0%	*38.0%*	*38.0%*	*38.0%*	*38.0%*
Other Convertible Preferred, other securities transactions	(1,069)	(388)	(396)	(55)	(50)	(45)	(40)	(190)	-	-	-	-
Net Income (Loss) - Effective taxed	**(12,389)**	**(20,832)**	**(6,452)**	**(7,005)**	**(6,490)**	**(6,830)**	**(4,930)**	$ (25,255)	**(9,350)**	**(18,375)**	**5,952**	**98,225**
Income - Fully taxed	(7,018)	(12,675)	(3,755)	(4,309)	(4,043)	(4,207)	(3,032)	$ (15,590)	(5,797)	(11,393)	3,968	66,557
Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Other Comprehensive Income (Loss)	16	(5)	(1)	(8)	-	-	-	(8)	-	-	-	-
Comprehensive Income (Loss)	(11,304)	(20,449)	(6,057)	(6,958)	(6,440)	(6,785)	(4,890)	$ (25,073)	(9,350)	(18,375)	6,400	107,350
EPS (ex-charges; eff. taxed)	**($9.66)**	**($16.15)**	**($4.99)**	**($0.76)**	**($0.37)**	**($0.38)**	**($0.28)**	**($1.61)**	**($0.52)**	**($1.02)**	**$0.31**	**$5.15**
EPS (ex-charges; fully-taxed)	**($5.47)**	**($9.83)**	**($2.91)**	**($0.47)**	**($0.23)**	**($0.24)**	**($0.17)**	**($1.00)**	**($0.32)**	**($0.63)**	**$0.21**	**$3.44**
EPS - comprehensive Income (eff taxes)	($8.81)	($15.85)	($4.69)	($0.76)	($0.36)	($0.38)	($0.27)	($1.60)	($0.52)	($1.02)	$0.33	$5.54
Shares O/S (000), Basic	1,283	1,290	1,292	9,188	17,750	17,800	17,850	15,647	17,875	17,975	18,975	19,075
Shares O/S (000), Diluted	1,283	1,290	1,292	9,188	17,750	17,800	17,850	15,647	17,875	17,975	19,275	19,375
					-- Expenses (% of sales) --							
Cost of Sales (product sales)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	NM	NM	NM
Gross	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
R & D	NM	NM	NM	NM	NM	NM	NM	NM	96.4%	134.8%	60.3%	21.6%
S G & A	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%
Total	158.3%	244.8%	117.4%	504.2%	420.0%	400.0%	207.8%	336.6%	132.7%	180.7%	86.4%	34.0%
					-- Year / Year Growth --							
Revenue	NM	NM	NM	NM	NM	NM	NM	NM	96.4%	-19.1%	123.6%	225.1%
Operating Income	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Pretax Income	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Income	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
EPS (ex-charges)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
EPS (ex-charges; fully-taxed)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM

Source: Concert Pharmeceuticals Inc. SEC documents and Ladenburg Thalmann BioPharmaceuticals estimates.

Contact Information: Robert (Bert) Hazlett, Managing Director, Ladenburg Thalmann, rhazlett@ladenburg.com, 212-409-2062.

Concert Pharmaceuticals, Inc.

Balance Sheet & Statement of Cash Flow ($mm)

	12/31/2011A	12/31/2012A	12/31/2013A	12/31/2014E	12/31/2015E	12/31/2016E	12/31/2017E
BALANCE SHEET							
ASSETS							
Cash & equivalents	$22.9	$7.5	$9.6	$69.3	$78.7	$77.5	$80.0
Investments/Mktb. Securities	$19.7	$20.1	$23.0	$23.0	$23.0	$23.0	$23.0
Account receivable	$0.6	$0.1	$0.3	$2.1	$4.1	$3.3	$7.5
Prepaid & other current assets	$0.9	$1.2	$1.1	$0.1	$0.3	$0.2	$0.5
Total Current Assets	$44.1	$28.9	$34.0	$94.6	$106.1	$104.1	$111.0
Property & Equipment, net, other	$4.4	$3.5	$2.5	$2.5	$2.5	$2.5	$2.5
Long term investment/Restricted Cash	$0.0	$0.0	$0.7	$0.7	$0.7	$0.7	$0.7
Other Assets	$0.8	$0.8	$2.5	$2.5	$2.5	$2.5	$2.5
Total Assets	**$49.4**	**$33.1**	**$39.8**	**$100.3**	**$111.9**	**$109.8**	**$116.7**
LIABILITIES & S.E.							
Accounts payable	$1.6	$0.8	$1.0	$1.4	$2.8	$3.3	$7.5
Accrued expenses	$1.5	$2.0	$2.5	$2.7	$2.9	$3.1	$3.4
Deferred short-term revenue	$6.9	$0.0	$4.3	$1.0	$0.0	$0.0	$0.0
Leasehold improvement loan	$0.3	$0.3	$0.3	$0.3	$0.3	$0.3	$0.3
Loans payable, net of discount	$0.0	$4.8	$7.8	$5.6	$8.3	$3.3	$10.0
Total Current Liabilities	$10.3	$7.9	$15.9	$11.0	$14.2	$10.1	$21.1
Deferrred revenue, net of current	$4.1	$2.8	$15.3	$9.0	$3.0	$0.0	$0.0
Leasehold improvement loan, net of current	$0.9	$0.6	$0.2	$2.0	$2.0	$2.0	$2.0
Deferred lease incentive	$1.4	$0.9	$0.4	$2.0	$2.0	$2.0	$2.0
Deferred rent, net of current	$0.6	$0.5	$0.2	$2.0	$2.0	$2.0	$2.0
Warrant to purchase redeemable securities	$0.2	$0.5	$0.5	$0.5	$0.5	$0.5	$0.5
Note Payable/Long-term Liabilities	$7.1	$14.9	$7.1	$7.1	$7.1	$7.1	$7.1
Total Liabilities	$24.7	$28.0	$39.6	$33.6	$30.8	$23.7	$34.7
Total Shareholders Equity	$24.7	$5.2	$0.1	$66.7	$81.1	$86.1	$82.0
Total Liabilities and Shareholders Equity	**$49.4**	**$33.1**	**$39.8**	**$100.3**	**$111.9**	**$109.8**	**$116.7**

	12/31/2011A	12/31/2012A	12/31/2013A	12/31/2014E	12/31/2015E	12/31/2016E	12/31/2017E
CASH FLOW STATEMENT							
Cash Flow from Operating Activities							
Net income (loss)	(11.3)	($20.4)	(6.1)	(20.3)	(9.4)	(18.4)	6.4
Other adjustments	0.0	$0.0	0.0	0.0	20.0	20.0	(15.0)
Depreciation & Amortization	1.6	$1.5	1.3	1.1	1.2	1.4	2.0
Noncash compensation expense	0.9	$0.9	1.0	1.0	1.5	2.0	2.5
Other non-cash financing expense	0.8	$0.4	0.3	0.0	0.0	0.0	0.0
Amortization of financing costs, warrants	(0.5)	($0.1)	(0.4)	0.0	0.0	0.0	0.0
Accounts receivable	1.0	$0.5	(0.2)	(1.8)	(2.0)	0.8	(4.1)
Interest receivable	0.1	$0.0	0.0	0.0	0.0	0.0	0.0
Prepaid expenses, and other current assets	(0.0)	($0.4)	0.0	1.0	(0.1)	0.1	(0.3)
Other assets	(0.1)	$0.0	0.1	0.0	0.0	0.0	0.0
Accounts payable and accrued expenses	0.7	($0.3)	0.1	0.6	1.6	0.8	4.4
Other oper.activities (deferred rent, revenue)	(11.2)	($8.4)	16.7	(8.5)	(3.4)	(7.9)	6.6
Cash Flow from Operating Activities	**(18.1)**	**(26.4)**	**13.0**	**(26.9)**	**9.4**	**(1.2)**	**2.5**
Cash Flow from Investing Activities							
Maturities of Investments	64	$37.7	27	0	0	0	0
Purchase of investments	(41)	($38.4)	(30)	0	0	0	0
Capital Expenditures, net	(0.3)	($0.5)	(0.4)	0.0	0.0	0.0	0.0
Other	-	$0.0	-	-	-	-	-
	22.9	**(1.2)**	**(3.64)**	**0.00**	**0.00**	**0.00**	**0.00**
Cash Flow from Financing Activities							
Issuance of loan payable, net	7.3	$12.5	0	0	0	0	0
Principle pmts of loan payaable	0.0	$0.0	(5)	0	0	0	0
Repayment of leasehold impt loan	(0.3)	($0.3)	(0)	0	0	0	0
Proceeds from iss. of common stock (net)	0.0	$0.0	0	86.6	0.0	0.0	0.0
Proceeds/Retirement of Debt, Other	0.0	$0.0	0	0.0	0.0	0.0	0.0
Payment of IPO/offering costs	0.0	$0.0	(2)	0.0	0.0	0.0	0.0
Cash Flow from Financing Activities	**7.0**	**12.2**	**(7.2)**	**86.6**	**0.0**	**0.0**	**0.0**
Beginning cash balance	**11.1**	**$22.9**	**7.5**	**9.6**	**69.3**	**78.7**	**77.5**
Net increase (decrease) in cash	11.8	($15.5)	2.1	59.7	9.4	(1.2)	2.5
Ending cash balance	**22.9**	**7.5**	**9.6**	**69.3**	**78.7**	**77.5**	**80.0**

Source: **Concert Pharmeceuticals Inc. SEC documents and Ladenburg Thalmann BioPharmaceuticals estimates.**

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APPENDIX A: IMPORTANT RESEARCH DISCLOSURES

ANALYST CERTIFICATION

I, Robert C. Hazlett, attest that the views expressed in this research report accurately reflect my personal views about the subject security and issuer. Furthermore, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report, provided, however, that:

The research analyst primarily responsible for the preparation of this research report has or will receive compensation based upon various factors, including the volume of trading at the firm in the subject security, as well as the firm's total revenues, a portion of which is generated by investment banking activities.

Additional information regarding the contents of this publication will be furnished upon request. Please contact Ladenburg Thalmann, Compliance Department, 570 Lexington Avenue, 11th floor, New York, New York 10022 (or call 212-409-2000) for any information regarding current disclosures, and where applicable, relevant price charts, in regard to companies that are the subject of this research report.

COMPANY BACKGROUND

Concert Pharmaceuticals, founded in 2006 by Richard Aldrich, Roger Tung, and Christoph Westphal, creates novel medicines by applying its DCE (Deuterated Chemical Entity) Platform technologies to molecules. The DCE approach involves the selective addition of deuterium, a stable isotope of hydrogen, to molecules, resulting in clinical therapeutic candidates with improved pharmacology. This approach has the potential to enable more efficient drug discovery and clinical development. Concert's proprietary programs include CTP-354, a novel GABA-A modulator for spasticity and anxiety, and CTP-499, a PDE inhibitor for diabetic kidney disease. Promising partnered programs include Jazz's JZP-386, a long-acting Xyrem, Avanir's AVP-786, an improved Neudexta, and multiple programs with Celgene. Concert has also developed a broad portfolio of deuterated molecules that are expected to migrate into and through the clinic over time.

VALUATION METHODOLOGY

Concert Pharmaceuticals Valuation. Concert and CNCE Shares Valuation. Because Concert's operations have the potential for significant revenue and earnings variability over the coming quarters and years, we value the company and its assets using a fully-taxed, risk-weighted net present value methodology for each of its assets. We note that with its multiple partnerships and emerging clinical programs, Concert has a diverse portfolio that contributes to its valuation. Our total of the programs yield a value of $24.20 per CNCE share, driving our $24 CNCE shares price target.

Concert's Proprietary Pipeline. Concert's two most advanced proprietary assets, CTP-354 for spasticity, and CTP-499 for diabetic kidney disease, have material valuation. CTP-354 for spasticity as a result of multiple sclerosis and/or spinal cord injury and possibly other indications such as anxiety and neuropathic pain, is moving into Phase 2. We believe that a GABA-A modulator with familiar mechanism, yet a distinct profile, with once-daily dosing and less sedation, should have material potential for consideration in spasticity, anxiety, and even pain settings, and have the potential to exceed $1 billion in peak revenue; we value its collective opportunities at $7.17 per share. CTP-499, for diabetic kidney disease appears to have achieved material validation after a more full analysis of its Phase 2 trial data, which bodes well for Phase 3 consideration. We assume international licensing should be able to occur after discussions with FDA of their end of Phase 2 meetings in 2H14, and that could be a validating event for the CTP-499 program. We estimate CTP-499 at $1 billion peak revenue in the US, despite risks to the endpoints that remain, value the program at $5.16 per CNCE share. Other less mature proprietary products are much more modest opportunities at this point and valued at $0.31 per CNCE share, though proof of concept comes at Phase 1 for many of these deuterated programs, and this part of the portfolio could appreciate quite quickly.

Concert's Collaborations. Regarding Concert's partnered portfolio, Avanir seems to be operating with a good urgency with AVP-786, and is exploring dextromethorphan's broad neurotransmitter receptor activity with the molecule, looking at the therapy in multiple additional indications in addition to depression, including agitation and dyskinesia. Because of these multiple indications, and its potential for its rapid advancement, the economics of this program are valued at $3.87 per CNCE share. The Jazz program JZP-386 attempts to provide the Xyrem franchise with a product that doesn't have middle of the night dosing, and can help protect against potential loss of exclusivity. Xyrem is growing rapidly (+50% yr/yr) and is large at $569 million annually, and making a more convenient dosing form with longer patent life appears to be a materially opportunity, generating a $2.37 NPV per CNCE share. Finally, Celgene has not disclosed what the mechanism of CTP-730 inflammation collaboration, though the very large regulatory milestones and peak revenue along the lines of Xyrem, give this collaboration a $3.61 NPV. The remainder of the Celgene assets are estimated at $0.58, and net cash, NOLs and the drag of general corporate expense totals ($4.15) per CNCE share, yielding the $24.20 total, driving our $24 CNCE shares price target.

Factors which could impede CNCE shares from reaching our price target include the lack of progress for Concert's proprietary therapeutics CTP-499 and CTP-354 in their respective indications. Progress by indirect competition in indications for chronic kidney failure or spasticity could also impede CNCE shares from reaching our target. Concert has a number of partnered programs, including efforts with Celgene, Jazz Pharmaceuticals, and Avanir, and there is no guarantee those programs will progress at all or in a way that is beneficial to Concert; a lack of progress with any or all of these partnered programs could be an impediment to CNCE shares reaching our target price. In addition, negative

equity market conditions overall, or in particular with regard to the biotechnology sector, or healthcare in general, could be an impediment to CNCE shares reaching our target. Also a change in the regulatory requirements for drugs in development could be an impediment to the advancement in CNCE shares. These risks listed are merely a sample of the types of issues that could impede CNCE shares from advancing, and are not meant to be all inclusive.

RISKS

Regulatory/FDA. As with any company whose main business focuses on the development of pharmaceuticals, Concert is subject to the strenuous regulatory requirements of the US Food and Drug Administration (FDA) and other international regulatory agencies such as the EMEA to have its new drugs approved. Promotion of its approved drug products is also highly regulated by FDA and related agencies throughout the globe.

Dependence on Proprietary Programs. CTP-354 and CTP-499 are two of Concert's most advanced proprietary clinical candidates in development. These novel molecules may take material time and resources to finish clinical development, if they are able to complete is at all, and there is certainly no guarantee that the company will be successful in doing so. In addition, Concert may seek one or more collaborators for future development of CTP-499. There is a risk that the company may not be able to enter into a collaboration for the therapy, or is able to enter into one with terms that are beneficial to CNCE shareholders.

Risks With Partnered Programs. Concert has a number of partnered programs, including material efforts with Celgene, Jazz Pharmaceuticals, and Avanir Pharmaceuticals. Because these programs are ultimately under the direction of other companies, there is no guarantee those programs will progress at all, or in a way that is beneficial to Concert or CNCE shareholders.

Deuteration: Approval, Manufacturing Risks. To the best of our knowledge, no deuterated drug has ever been successfully approved or commercialized. There may be specific risks to gaining licensure for these types of agents from regulatory authorities, though these do not appear to have not emerged at this point.

STOCK RATING DEFINITIONS

Buy: The stock's return is expected to exceed 12.5% over the next twelve months.

Neutral: The stock's return is expected to be plus or minus 12.5% over the next twelve months.

Sell: The stock's return is expected to be negative 12.5% or more over the next twelve months.

Investment Ratings are determined by the ranges described above at the time of initiation of coverage, a change in risk, or a change in target price. At other times, the expected returns may fall outside of these ranges because of price movement and/or volatility. Such interim deviations from specified ranges will be permitted but will become subject to review.

RATINGS DISPERSION AND BANKING RELATIONSHIPS AS OF (July 21, 2014)

Rating	%	IB %
BUY	75.4	57.3
NEUTRAL	24.6	40.8
SELL	0.0	0.0

COMPANIES UNDER ROBERT'S COVERAGE

Acadia Pharmaceuticals Inc. (ACAD)
CTI BioPharma Corp. (CTIC)
Prothena Corporation plc (PRTA)
Concert Pharmaceuticals Inc. (CNCE)
Nektar Therapeutics (NKTR)
Targacept, Inc. (TRGT)

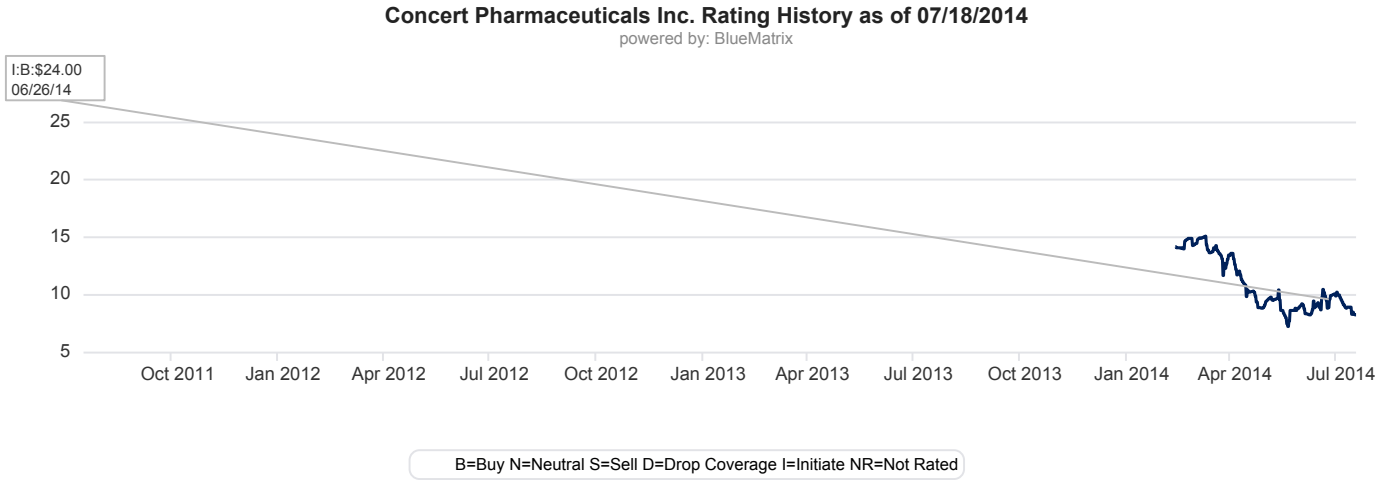
COMPANY SPECIFIC DISCLOSURES

Ladenburg Thalmann & Co. Inc. makes a market in Concert Pharmaceuticals Inc..

Ladenburg Thalmann & Co. Inc. intends to seek compensation for investment banking and/or advisory services from Concert Pharmaceuticals Inc. within the next 3 months.

OTHER COMPANIES MENTIONED

INVESTMENT RATING AND PRICE TARGET HISTORY



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