

Elan's Tale: Was Not a Journey More Imposing?

By Chris Chan

Genesis and Metamorphosis

All who 'cross this fair land live,
Stay and hear these words I give:
A tale of bitter tragedy
Entwined with hope and ecstasy.
The quest for Phrixus' Golden Fleece
By Jason, son of ancient Greece,
Was not a journey more imposing
Than Elan's tale, I'm supposing.

She started as a company
Sole-focused on delivery
Of drugs too difficult digested:
For this we in Elan invested.
Perchance one day the Irish gent
Named Donal formed the bold intent
To broaden wide Elan's vast realm.
And so with Donal at the helm,
Elan her empire expanded
(As her lofty goal demanded).

Thus arrived Athena fair
A virgin orb wondrous and rare;
Her price need no apology,
This nugget of neurology.
That she possessed technology
Robust was no mythology.¹
So Elan other firms acquiring
Achieved the size she was desiring;
The golden age did thus arrive –
A summit reached at sixty-five.²

The Fall I

But then both hell and Hades stirred,
A frightful raging storm occurred;
As if all angry force conspired
Against this firm we most admired.

First fretful winds of ill befell
The elixir that sought to quell
Those ailments that invade one's brain
And cause near-endless woe and pain.
E'en as it helped the brain avoid

Its harmful beta amyloid,
Succumbed a few to ills adverse;
Thus trial did cease, for fear of worse.³

And while Elan reeled from this blow,
Another tempest did then grow:
Claims of income much inflated
Led by partners false created.
Alas a world of Enronitis⁴
Caused a stampede at the slightest
Hint of bloated earnings smell;
Amidst this shadow Elan fell.
Then stirred the restless SEC
Those ruling titans from DC,
From their thrones investigated
All that our Elan had stated.⁵

With shorting vultures sensing blood,
The selling tide became a flood;
And doomsday prophets salivated
At that end Elan seemed fated.
As confidence maintained its slip,
The captain forced to leave his ship:
A victim of his goals aggressive
Suddenly deemed too excessive.⁶

The Arising Phoenix I

So like a dreaded sickness viral
Towards sad end all seemed to spiral,
When then up stood amidst the harrow
He who others knew as Garo.
Shouted he to all who heard,
"Demise concerns are most absurd!
We've still rich assets – that's a fact.
A planned recovery we'll enact."⁷

Thus with commitment strong and true
Elan resolved to start anew:
First long-term health she must protect
By paring low her fearsome debt.
The choice was made which parts to sell;
What prices fetched – but time would tell.
The naysayers all hemmed and hawed,
Proclaimed they this strategy flawed:
"This can but make small dent," they sneered.
But heedless Elan persevered.

Like amorous beasts the suitors came,
Their bids surpassed the seller's aim.
Rather than small ducats bring,
Came princely ransoms fit for King.⁸
Observers marveled at the offers

And their boon to Elan's coffers.
But perhaps most importantly
Elan held fast her jewels three:
The programs for dementia stayed
As did the valued MS aid;
Her nanotech she need not sell;
Onto this gem she kept as well.
Thus step by step with fate's kind kiss,
Away she strolled from the abyss.
With one limb trenched within the grave
Managed Elan herself to save.

Amidst this time of fog and grind,
A captain new she sought to find.
But who to head this firm "beleaguered?"
Perhaps a Wall Street vet, she figured.
So onto Elan's narrow plank
Walked the man from Merrill's bank.
And thus arrived the age of Kelly
To light the fire in Elan's belly.⁹

Immediate he set to chore
The faith of Elan's books restore;
Some debt refinance he pursued
And all "death spiral" fears subdued.
But lingered still like pit bull's fang,
A stiff SEC overhang;
Eons they seemingly took
To close examine Elan's book.
(A wounded tortoise would succeed
In moving at a greater speed.)
Fed up with slow bureaucracy,
Rose then the famous brave souls three:
JT, Kungpo and Lovesjohndory
Achieved their place in Elan's story.¹⁰
Amidst the swirling winds they stood
Within that busy neighborhood
Where SEC's headquarters lay;
To all who passed they gave their say
With picket signs both bright and loud
Above their heads held high and proud.
Proclaimed the message of their creed:
"From this snail's clutch we must be freed!"
Perhaps spurred by this trio's mettle,
The case shortly thereafter settled.

The Miracle Elixir

Then came a happy era brief
(Much to her shareholders' relief).
Recover efforts fruit did yield
As wounded balance sheet was healed.
Anon a shiny beacon beamed-

A monoclonal star that gleamed
Across the mounts and seven seas
This potion for immune disease.
The data showed (in case you missed it)
Twice as good as what existed!¹¹
Surely lands of unmet need
Required this elixir indeed.
The Food and Drug lords then decided
Soon Tysabri be provided
To relapsing patients needy:
Approval nod must thus be speedy.
Thus swifter than was ever done
Permission granted at year one.¹²

Relapsing patients joyfully
Bid welcome to their Tysabri;
So as the drug was wider used
And greater numbers were infused,
More tales of grand results emerged
Of disabilities it purged.¹³
The ones who at infusion's wake
Were able to wheelchair forsake;
While she who small lengths could not hike,
Miles she then pedaled on her bike.
In this bright light, demand was high
And multitudes received their Ty;
Apart from these, more than a few
Eager awaited in the queue.

Hence once again Elan flew high
Upon the wings of treasures nigh.
Again the fickle Street did grace
Elan with its lustful embrace.
Yet on these smiling days so warm
Did land another tragic storm....¹⁴

The Fall II

Upon a Monday Black it fell,
The second devastating hell.
'Twas learned a trial patient pair
Contracted both an ailment rare;
From PML one passed away,
The other in deep sickness lay.
Were others with MS surmised
In truth with PML disguised?
These answers Elan did not have
In that saddened aftermath.
So with her Cambridge partner and
Implicit FDA command,
Tysabri from the world removed
Just months from when 'twas first approved.¹⁵
This action heavily debated,

Patients were all devastated
As were those who her shares owned,
Yet once again punished and stoned.
Amidst the anguish and confusion
O'er the fate of this infusion,
Word arrived of patient three
Misdiagnosed previously.¹⁶

At once the faithless hordes all shouted,
Cursed the gem that they now doubted
Back to light ever return;
Their passing fancy turned to spurn.

As Elan hung on feeble branch
In face of crushing avalanche,
The Boston scribe then shook the tree
And added to her misery.
Proclaimed the Globe of one case more:
The "death" of patient number four.¹⁷
Surely 'tis the final blow
That lays Elan's Tysabri low.
Again observers last rites read,
Elan and potion left for dead;
For even the most faithful true
Must now admit the story's through!

The Rising Phoenix II

But like cold darkness ere the dawn,
A breath of light does slowly spawn
To grant sweet warmth on those who cope
And through the black night dare to hope.

First word emerged that "patient four,"
Far from deceased, was at the store
When news was spread of her heart stopping;
Undaunted, she continued shopping.¹⁸

The partners two to us did mention
Ty redeemed was their intention.
Captain Martin proclaimed then
Return of Ty - "not if but when."
Commenced they then evaluation
Of all who had participation
In our potion's trials days past,
Until Tysabri's cleared at last.

As slow months passed t'ward end of year
To us it seemed abundant clear,
No further case would they tell
Of patients who have PML.
At final tally came the word:
Two passed away; survived the third.

Of all three cases to arise,
All three had systems compromised:
Two with Avonex injected,
The third – immuno drugs detected.
Important most, none of the three
Received Ty monotherapy.¹⁹
With data from all patients tested,
Return of Ty the firms requested;
To FDA they did implore
Priority review once more.
Once the lords did grant this blessing,
Thoughts then focused on addressing
Challenges they'll surely greet
When Ty's Advise Committee meets.

A day in chilly March they met
Arrived by buses, train, and jet
MS patients coast to coast
To fight for what they wanted most.
This meeting of the committee
To deem the fate of Tysabri,
Could scarce fit all the crowd inside
And those who sought to testify.
To please all those who wanted say,
The meet did add a second day.
Then one by one they stood and spoke,
More than a tear they did provoke
With stories of their MS tragic,
A short time helped with Tysab's magic.
Like Cheryl, Lauren and Mike Barron
To healers for their patients caring,
All entreated with one voice
To have Tysabri as a choice.
Before the day to dusk did sail,
Over forty told their tale.²⁰
As testimonies all subsided,
The experts viewed data provided;
Then to their talking rooms adjourned
Until the verdict was returned:

Tysabri filled an unmet need,
Effective for MS indeed!
Back to market it must speed,
Unanimous they all agreed.²¹

And so it passed at three months hence
Ty sales were let to re-commence
Just fourteen months after convicted
By prophets who its death predicted.²²

Though uptake slow as walking crutch
Because of new requirements TOUCH,
The patients all rejoiced and waited

For their turns anticipated.
But yet naysayers did regroup
And sneered aloud at Elan's coup:
Although this drug returns anew,
Its users will be very few!
The fear of PML, they claim
Would surely sales of Tysab tame.
What doctor would this drug prescribe
And risk a lawyer's diatribe?
Yet as they limit Ty's projection
(Could some intent be CRAB's protection?)²³
Patients once more set in motion,
Lining up for this sweet potion;
Glad to bear the risk and strife
For improved quality of life.

The Future

Meanwhile, Elan's main design-
To remedy demented mind;
With partner Wyeth did progress
And inch e'er closer to success.
The compound bapineuzumab
(A product of Athena's lab)
Speeds through her trials clinical
For AD treatment's pinnacle.
It clears brain's store of plaque supplies
In patients passive immunized.
As for immunization active,
ACC appears attractive:
To clear the beta amyloid,
One's own immune response employed.
The program Beta Secretase
May one day earn physicians' praise,
And Gamma methodology,
May prove a key pathology.²⁴
For treatments we'll all one day want,
Elan's great science stands in front.

Epilogue

What future brings we must now wait
It rests in hands of fickle fate;
But sure as lions stalk their meal,
All doters on Elan will feel
At times great joy, at times frustration,
If the past is indication.
Twice before near final throes,
But then like Lazarus she rose
Refusing to give up the fight
And gentle go to that good night.
So now beyond the storms and sleet,
Will she her vast potential meet?

Like Frodo to Sam Gamgee swore,
There are still several chapters more.

Notes

1. In March 1996, Elan announced its intention to buy South San Francisco-based Athena Neurosciences Inc for \$625M. Athena would provide what would ultimately prove to be some of Elan's most important pipeline products, including Tysabri and the Alzheimer's programs.
2. On June 20, 2001, Elan (ELN) closed at its all-time high of \$65 a share.
3. In February 2002, Elan and partner Wyeth (at the time known as American Home Products) halted the Phase II trial of AN1792, a promising Alzheimer's vaccine treatment, when four patients in the trial developed meningoencephalitis. Ultimately, it was learned that 18 patients (or 6% of participants) developed this brain inflammation. Although dosing ceased, the companies continued to collect and evaluate data from the trial. The data suggested the immunotherapy approach of AN1792 was indeed promising, and this ultimately led to Elan and Wyeth's "next generation" potential treatments for Alzheimer's, including AAB-001 (passive immunization) and ACC-001 (active immunization).
4. This was during the time when a number of big companies were brought down by accounting shenanigans, including Enron, Worldcom and Global Crossing. When it initially came to light that Elan used off-balance sheet financial vehicles known as "Special Purpose Entities (SPE's), investors sold first and asked questions later. SPE's were one of the more publicized instruments used (and abused) by Enron.
5. In February 2002, the SEC announced an investigation into Elan's accounting practices after a Wall Street Journal article questioned how the company accounted for revenues from numerous joint-venture research partnerships.
6. In July 2002, amid a plummeting of the stock price, Donal Geaney and Tom Lynch resigned their positions as Elan's CEO and CFO, respectively. They both retained consultant positions with Elan for some time afterwards.
7. After Donal Geaney and Tom Lynch's departures, Garo Armen, CEO of biotech Antigenics, Inc. and Elan board member, took over as Chairman and Interim CEO of Elan. In November 2002, he said in an interview with The Sunday Business Post that Elan would survive the crisis because asset sales would yield attractive prices and because "amidst all the problems we have a very impressive pipeline – real science."
8. Many of Elan's assets sold at higher prices than analysts projected. The most significant sale was King Pharmaceuticals' bid of \$850M for two Elan products: muscle relaxant Skelaxin and insomnia drug Sonata (plus a 400-person sales force). King later attempted to renege on the deal, and Elan sued. The case was soon settled, with King agreeing to pay \$750M plus additional royalties and milestone payments. Because of the prices Elan obtained, it was able to keep the drug delivery unit, which many speculated would be sold as part of the recovery plan.
9. In January 2003, Elan hired Kelly Martin (KM) as president and CEO. KM had worked for 21 years at Merrill Lynch, most recently as head of the international brokerage entity.
10. Fed up with the slow pace of the SEC investigation, three Elan shareholders (known on Elan's very active message board as Jtinformed, Kungpostyle and Lovesjohndory) picketed outside the SEC building to bring attention to the fact that the slow pace was potentially harming shareholders as well as study patients. During the course of the protest, a fourth picketer briefly joined the heroes – a homeless man who just wanted to feel like he belonged. This was just one of many active (but unsanctioned) shareholder efforts on behalf of Elan's interests. For instance, Lovesjohndory, a lawyer by profession, later attended the court proceedings in which a judge determined what amount of the shareholders' lawsuit settlement the class-action lawyers should receive.

Noting that the class-action lawyers did nothing more than cut and paste allegations printed in the media (and sloppily at that), Lovesjohndory argued that their cut of the pie should be minimal. The class action lawyers asked for 25% of the settlement (or \$19M), but the judge ultimately awarded them \$9M (12%). Subsequent rumor has it that numerous Lovesjohndory voodoo dolls began showing up in class action lawyer offices.

11. Phase III trial data demonstrated that Tysabri reduced MS relapses over placebo by 67%, while existing MS treatments in the market generally showed relapse reduction over placebo of about half that percentage.
12. Although Tysabri's Phase III trials were designed as two-year studies, the FDA encouraged Elan and Biogen to submit for approval based on one-year data results. The companies would still complete both years of the trials, but approval could be granted much earlier than normal.
13. There were numerous anecdotal accounts of subjects achieving spectacular results from Tysabri. Later, those accounts seemed to gain significant credence when, in April 2006, Elan and Biogen-Iddec presented data at the American Academy of Neurology Annual Meeting that Tysabri demonstrated significant favorable effects on pre-specified health-related quality of life (QoL) measures in MS patients.
14. From a low close of \$1.05 on October 1, 2002 during the first "death spiral" storm, Elan rebounded to a \$29 close on January 12, 2005 primarily on the strength of Tysabri expectations. After the PML fiasco, Elan fell to as low as a \$3.00 on March 31, 2005.
15. On Monday February 28, 2005, the companies announced that Tysabri was being withdrawn from the market and clinical trials dosing halted because two subjects in the SENTINEL (Tysabri in combination with Avonex) trial contracted a very rare and often fatal infection known as progressive multifocal leukoencephalopathy, or PML. A few weeks later, a third case of PML was discovered in a former subject in the Tysabri Crohn's disease trial.
16. This third subject, a participant in a Tysabri Crohn's disease clinical trial, was originally diagnosed to have died from malignant astrocytoma (a type of brain tumor). During the companies' review and investigation in the wake of the PML cases, this subject was re-diagnosed as having died of PML.
17. On June 2, 2005, a Boston Globe headline trumpeted "A fourth death may be tied to Biogen's MS drug." The headline was later changed to "A fourth illness" after it was discovered that the subject wasn't dead. Still later, it was discovered that the subject never had PML; she had a more benign inflammation ailment. In fact, there has not been a "third" PML death associated with PML. To date, there have been two PML-related deaths linked to Tysabri use.
18. Upon hearing that the subject in question was reportedly dead, the subject's doctor was quoted as saying that the subject was "alive and out shopping."
19. Of the three PML cases linked to Tysabri use, two were given Tysabri in combination with Avonex. The third subject (from the Crohn's trial) was taking a number of other immunosuppressive treatments including azathioprine (Imuran), which itself has been directly linked to PML.
20. On March 7-8, 2006, an FDA advisory committee meeting for Tysabri was held in Gaithersburg, MD. Numerous MS patients spoke out on behalf of Tysabri's return, including some who testified via videotape because their MS disability prevented attendance at the meeting in person. Over three hours of testimony was given by over 40 patients, family members of patients, and doctors, all of whom requested that they be allowed the choice of taking Tysabri. Because so many people requested the opportunity to testify, a second day was added to the meeting.
21. In the end, after hearing all testimony and reviewing all relevant safety and efficacy data, the FDA advisory committee unanimously recommended that Tysabri be returned

to market as a monotherapy. They also voted 7 to 5 in favor of permitting doctors to prescribe Tysabri as a first-line treatment.

22. On June 5, 2006, the companies announced that the FDA approved the reintroduction of Tysabri as a monotherapy for relapsing forms of MS. In conjunction, a risk management plan called TOUCH ("Tysabri Outreach: Unified Commitment to Health") would be implemented, which included a revised label warning, mandatory program enrollment of all patients, prescribers, pharmacies, and infusion centers, centralized Tysabri distribution, and mandatory educational tools for doctors and patients.
23. CRABs is an acronym used to represent the current major available MS treatments in the market: Copaxone, Rebif, Avonex, and Betaseron. Some conspiracy theorists have alleged that certain analysts express pessimism over Tysabri's prospects because they are "in the pockets" of the drug companies that market CRABs.
24. Among Elan's current major Alzheimer's clinical research programs are: AAB-001 ("bapineuzumab"), a "passive" immunization approach to clear beta amyloid peptide in the brain ("passive immunization" means antibodies are provided directly into the patient, rather than injecting an agent that causes the body to create its own antibodies); ACC-001, an "active" immunization approach intended to induce a highly specific antibody response to beta amyloid; the Beta Secretase program, and the Gamma Secretase program.

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