U.S. demand forecast: Prolia® and Xgeva® 2013–2015

Rosie Oganesian



Amgen's core franchises are shrinking; denosumab is the growth engine

$15.1B	$4.6B	17,000+	10
2010 revenue	2010 net income	employees	U.S. approved drugs

- Founded 1980 as Applied Molecular Genetics; *renamed* Amgen in 1983
- **Headquarters:** Thousand Oaks, CA | **CEO:** Kevin W. Sharer
- **Core franchises:** Aranesp & Epogen (anemia), Enbrel (arthritis), Neulasta/Neupogen (neutropenia)

PRESSURE

- Core products not doing well; Aranesp fell 15% in 2009
- Patent expirations looming
- Stock slid from $85 (2005) to ~$55 (2010)
- **Denosumab is the growth engine**

Source: Forecasting Denosumab (Kellogg KEL531),
Amgen Inc., Q4 2010 earnings press release (January 24, 2011)



One Antibody, Two Products

RANK ligand inhibitor, it blocks the protein that activates osteoclasts, the cells that break down bone.
The first biologic antibody approved for osteoporosis.
Patents run 2017–2023.

Prolia®

Postmenopausal osteoporosis, bone breaks down faster than it rebuilds

DOSE 60 mg injection, every 6 months

PRICE $825/dose = $1,650 per year

EVIDENCE FREEDOM (n=7,868): vertebral −68%, hip −40%
65% preferred the shot

- 30.7M Americans with osteoporosis or osteopenia;
  - only 15.5M diagnosed, ~5.6M treated
- Generic alendronate holds 53% of prescriptions at $650/year
- 50% of patients discontinue oral therapy within a year

XGEVA®

Bone metastases from solid tumors, cancer spreads to bone, oncology

DOSE 120 mg injection, every 4 weeks

PRICE $1,650/month = $19,800 per year

EVIDENCE Superior to Zometa® in breast & prostate; noninferior in other solid tumors

- 380,000 potential U.S. patients w/ 238,000 untreated
- Zometa® is standard of care ($800M U.S.) but loses patent protection in 2013

Source: Forecasting Denosumab



The osteoporosis market is full. The oncology market isn't.

	OSTEOPOROSIS MARKET early stage → advanced therapies								ONCOLOGY MARKET	
	Fosamax®	**Generic alendronate**	**Actonel®**	**Boniva®**	**Prolia®**	**Reclast®**	**Evista®**	**Forteo®**	**Zometa®**	**Xgeva®**
Market share	1%	53%	15%	12%	**new**	8%	12%	1%	Only Competitor	**new**
Indication	Mod. fracture risk	Mod. fracture risk	Mod. fracture risk	Mod. fracture risk	**High risk, 2nd line**	High risk, 2nd line	High risk	Severe risk	Metastatic cancer	**Metastatic cancer**
Delivery Route	Home oral weekly	Home oral weekly	Home oral weekly	Home oral monthly	**Clinic inj. biannual**	Clinic inf. per 2 yrs	Home oral daily	Home inj. daily	Clinic infusion per 4 wks	**Clinic injection per 4 wks**
Annual cost	$1,144	$650	$1,664	$1,392	**$1,650**	$1,137	$1,606	$11,680	$10,900	**$19,800**
Side effects	GI Upset	GI Upset	GI Upset	GI Upset	**ONJ Risk**	—	Clots and Stroke	Cancer Risk, 2 year limit	Comparable adverse events	**Comparable adverse events**
Benefit Channel	Pharmacy Part D	Pharmacy Part D	Pharmacy Part D	Pharmacy Part D	**Part B**	Pharmacy Part D	Pharmacy Part D	Pharmacy Part D	Part B	**Part B**
Patent expiry	Epired 2008	—	2012	2012	**2017–2023**	—	2012	—	2013	**2017–2023**

Denosumab enters 2 very different fights:
Prolia® is priced above a $650 generic that already owns half the osteoporosis market, while Xgeva®® faces a single target it can beat on delivery

*Amgen products highlighted**

Positioning

	Prolia®	XGEVA®
	Primary Care ; Buy and Bill	**Oncology ; Buy and Bill.**
Threat of Substitutes	Generic alendronate at $650 holds 53% of scripts, plus 5 other branded options HIGH	Only Zometa®, but it goes generic in 2013 MODERATE
Buyer power (payers)	Part B buy and bill, but the osteoporosis category is Part D, PCPs don't stock drugs HIGH	Part B, buy and bill. Oncologists already manage drug inventory MODERATE
Competitive Rivalry	7 products already available in a saturated market HIGH	One competitor, and denosumab beat it in 2 trials LOW
New Entrants	No major osteoporosis launch expected for 5 years LOW	No comparable product expected for 5 years LOW
Supplier power	Assumption: Amgen manufactures denosumab internally LOW	Same LOW

PRESSING ISSUES

1. **Win payer access**
   Justify the premium over generics, convenience is key
2. **Prescription Manageability**
   Primary care has to buy Prolia® upfront and get reimbursed later; oncology already works this way
3. **Coverage needs to be won**
   Not every FDA approved drug gets reimbursed
4. **Patents**
   Zometa® loses patent protection in 2013

Source: Porter, the five competitive forces that shape strategy

Both products win on delivery & lose on price

	OSTEOPOROSIS — Prolia® vs. generic alendronate For high-risk postmenopausal women who can't stay on an oral, Prolia® delivers proven fracture reduction in two office visits a year instead of fifty-two doses she has to remember.	**ONCOLOGY - UROLOGY** — XGEVA® vs. Zometa® (zoledronic acid) For oncologists and urologists treating bone mets, Xgeva® delays skeletal events longer than Zometa® with a subcutaneous shot, no infusion chair or set up is needed.
Dosing frequency	Twice a year vs. weekly pills	Every 4 weeks — similar to Zometa®
Route	SC injection vs. oral tablet	SC injection vs. IV infusion
Efficacy	FREEDOM trial: vertebral fractures −68%	Delays skeletal events better than Zometa®
Adherence	Office given shot vs. 50% of patients who quit orals with a year	Both provider-administered
Price	~$1,650 vs. ~$650/yr generic	~1.8× the cost of Zometa®
Access	B&B in primary care vs. generic	Part B - Specialty clinics already administer
Safety	ONJ & rebound fracture risk if stopped	Comparable Adverse Events

Advantage Comparable Gap / trade-off

Access is decided by payers and prescribers, not by patients.

high

POWER →

low

KEEP SATISFIED

High power · Low interest

- Hospital systems who may be administering
- Group purchasing organizations who negotiate drug pricing
- CMS (coverage & reimbursement)
- Specialty pharmacies

MANAGE CLOSELY

High power · High interest

- Medicare Part B contractors and commercial medical benefit payers who control Xgeva® access
- Part B plans and PBMs who control Prolia®
- Oncologists and urologists: about 40% of prostate cancer patients see a urologist, and urologists don't have infusion suites
- PCPs and internists: see 20+ patients a day, but they don't carry drug inventory
- Rheumatologists and endocrinologists: high risk osteoporosis patients are seeing
- FDA

MONITOR

Low power · Low interest

- Patients intolerant of other osteoporosis therapies
- Media

KEEP INFORMED

Low power · High interest

- Postmenopausal women who've already quit an oral bisphosphonate
- Patient advocacy organizations
- Caregivers

low

high

INTEREST →

Source: Mendelow's power/interest grid .

Same Drug, 2 Channels

	Prolia® Osteoporosis · primary care	**XGEVA®** Bone metastases · oncology · urology
Product	60 mg subcutaneous shot, twice a year. First biologic approved for osteoporosis • a convenience over daily/weekly pills.	120 mg subcutaneous shot, every 4 weeks (about 13x a year). Superior to Zometa® in breast & prostate cancer • no IV infusion site needed.
Promotion	Large sales force detailing internists and rheumatologists, plus print advertising to primary care. DTC is an option given the population size, Boniva showed it works through online ads and TV .	Specialized oncology sales force; no consumer advertising.
Place	B&B Part B, given in the office. But the osteoporosis is Part D and primary care offices don't stock drugs.	B&B through oncology or urology practices, who already manage drug inventory. Reimbursed under Medicare Part B.
Price	**~$825 / dose → ~$1,650 per year**	**~$1,650 / month → ~$19,800 per year**
Competitor Pricing	***Generic alendronate is $650.***	***Zometa® is $10,900.***

2 Target Groups & Neither Are New Patients

Prolia® and Xgeva® launch into completely different patients groups
Woman who already quit oral medication & the other are patients who Zometa® didnt work for

	Prolia® • Denosumab				XGEVA® • Denosumab			
Diagnosis state	Low bone mass ~30.7M	Osteoporosis, undiagnosed ~5.2M	Diagnosed, never treated ~2.7M	**Diagnosed and on therapy ~1.53M**	Cancer, no bone involvement	Bone mets not yet found	Bone mets, no skeletal event	**Already had a skeletal event**
Patient Population	Premenopausal women	**Postmenopausal 50–64**	**Postmenopausal 65+**	Men over 50 ~2M	**Breast cancer ~151K**	**Prostate cancer ~135K**	Other solid tumors ~111K	Myeloma
Who prescribes	**PCPs and internists**	**Rheumatologists**	**Endocrinologists**	OBGYNs	**Community oncologists**	**Urologists**	Hospital and academic	
How it gets paid	**Medicare Part B**	**Commercial medical benefit**	Medicaid	Out of pocket	**Medicare Part B buy-and-bill**	**Commercial medical benefit**	Medicaid	Uninsured
Prior therapy	Never tried a bisphosphonate	On an oral and doing fine	**Quit it, or can't tolerate it**	**Fractured anyway**	Never on a bone agent	On Zometa® and tolerating it	**Skeletal event on Zometa®**	**On Zometa® no skeletal event**
What drives the decision	**Manages her own health closely**	**Busy & misses doses**	Only acts after a fracture	Not engaged	**Buy-and-bill margin matters**	Follows guidelines	Cost conscious, will defend Zometa®	Capitated or risk bearing

Goal to Launch at **Build toward** **Not a priority**

Teal shading carries the same meaning on the Xgeva®® side.

Launch here: ~600K women. Insured, diagnosed, over 50, and they already stopped an oral or fractured on one. Their PCP or rheumatologist sees them yearly.
Build toward: ~944K diagnosed but never started any treatment who are at a high fracture risk.

Margaret, 68. *Quit alendronate at month four because of reflux. Nobody re-treated her. Medicare Part B.*

Launch here: ~103K patients. Breast and prostate bone mets already on Zometa®. Denosumab beat it on time to first. The trials show denosumab delays the next one better. Community oncologists and urologists buy and bill.
Build toward: ~238K with bone mets on no SRE therapy at all.

Robert, 71. *Prostate cancer in the bone, two years of Zometa®, then a spine fracture anyway. His oncologist switched him the same visit. Medicare Part B.*

What drives the demand

Only half of osteoporosis patients are diagnosed, and 63% of bone metastases patients get no SRE therapy at all

Macro

1 Eligible population

Prolia®

10M Americans have osteoporosis only; 30.7M include osteopenia

XGEVA

380,000 U.S. cancer patients have bone metastases from solid tumors

2 Diagnosis rate

Prolia®

Only 15.5M of 30.7M are diagnosed (50.5%); the disease is silent until a bone fracture

XGEVA

Found on bone scan, X-ray, or MRI ; usually only after the patient reports pain

3 Competitor price and patent loss

Prolia®

Generic alendronate holds 53% of prescriptions at $650/yr vs $1650 for Prolia®

XGEVA

$19,800/yr vs. $10,900 for Zometa®, which loses patent protection in 2013

Micro

4 Treatment rate

Prolia®

5.6M are on any therapy; Amgen estimates half of osteoporosis patients get nothing

XGEVA

238,000 of 380,000 receive no SRE therapy at all — the growth pool

5 Payer channel and site of care

Prolia®

PCPs and internists do not carry inventory; buy-and-bill is still a new terriority for them

XGEVA

Oncologists buy and bill routinely; urologists can treat without an infusion suite

6 Persistence and doses per year

Prolia®

2 doses a year and half of oral bisphosphonate patients quit within 12 months

XGEVA

12 to 13 doses a year, continuing until the patient stops active treatment

Source Calkins & Aggarwal (2011), Forecasting Denosumab, KEL531, School of Management.

Capture share from unmet need first

The clearest opportunities come from under treated patients, therapy failure, and switching.

1) Prolia® : switch + high risk starts

Target women already diagnosed who are failing current therapy and high risk untreated patients. The six month injection is easier than weekly pills, PCP limits uptake.

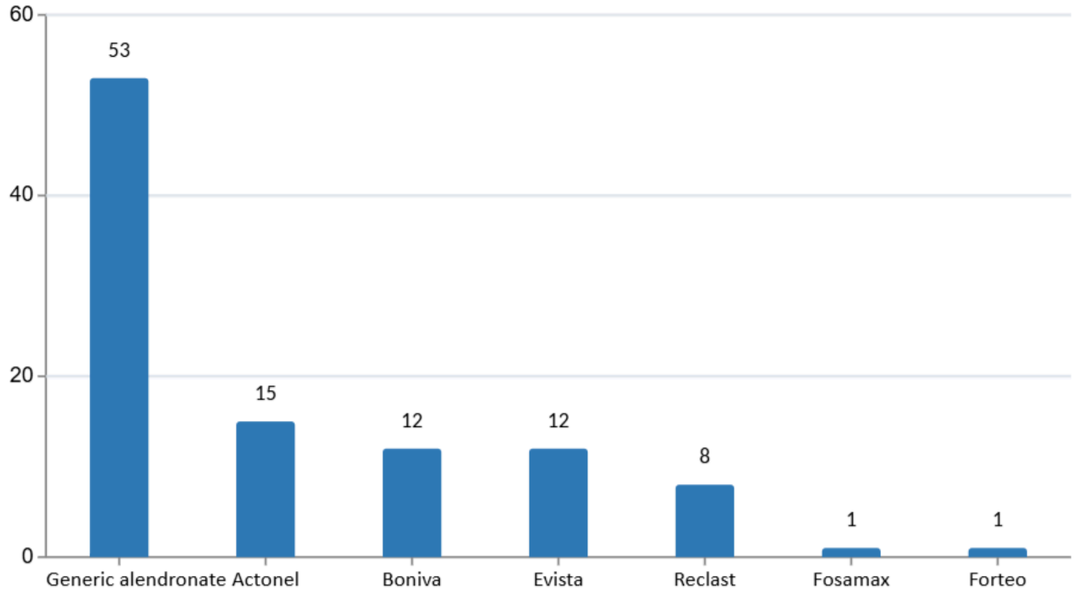
2) Xgeva®® : untreated bone metastases

The oncology market has a bigger immediate gap: 238,000 of 380,000 bone metastases patients weren't on Zometa® and oncologists are already comfortable with B&B

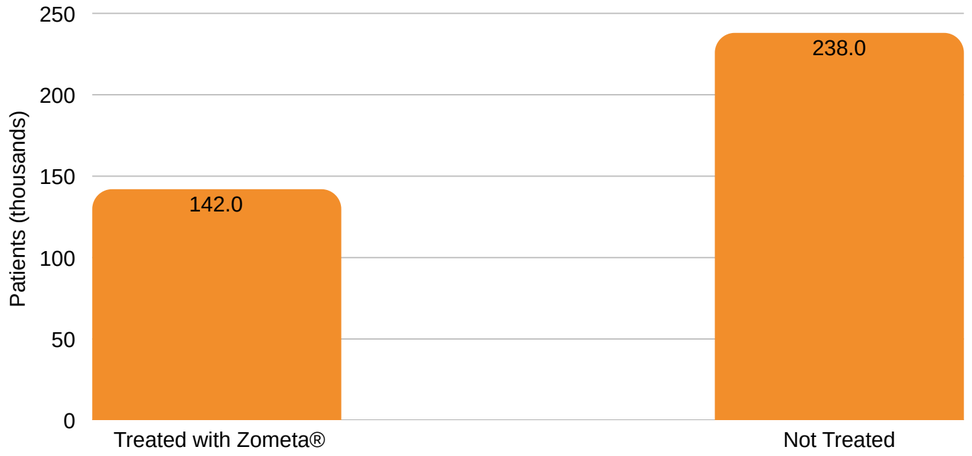
3) New indication = Prevention

Prevention in prostate cancer is the optional upside. Study 147 showed denosumab prevents bone metastases in nonmet prostate cancer (p. 11). Assume 50% approval odds

Osteoporosis market share is hard to move because generics are leading



Bone metastases starts with a larger untreated gap

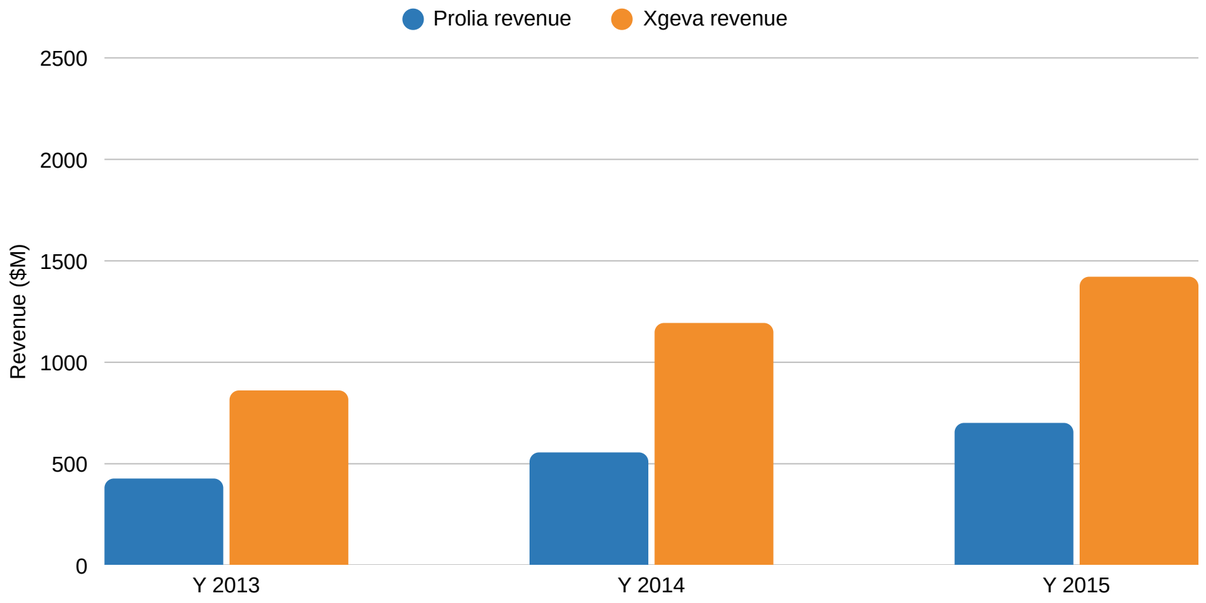


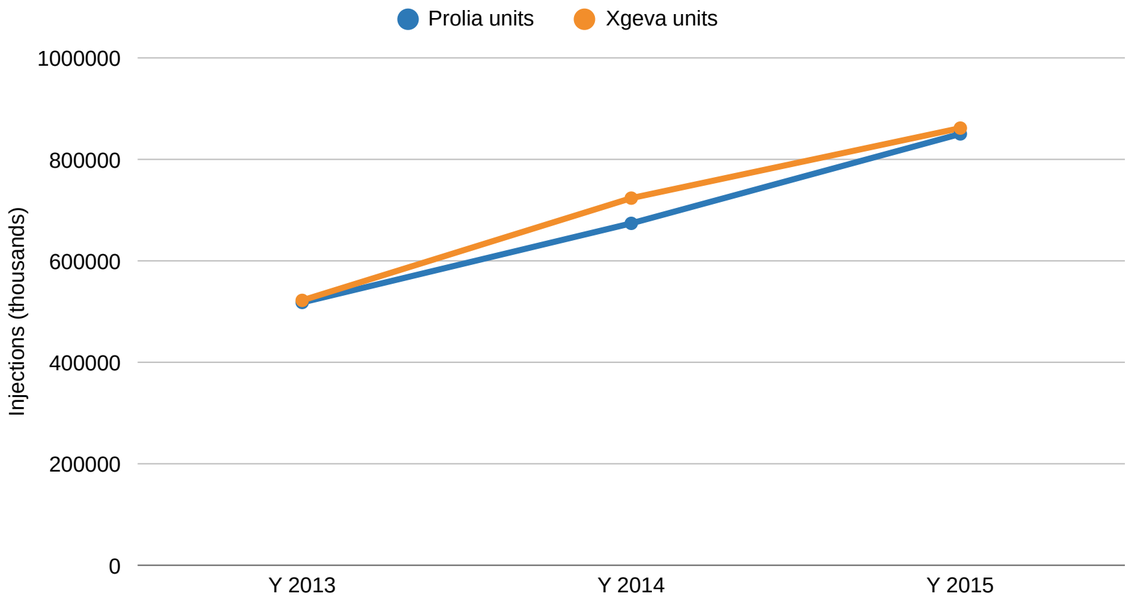
Takeaway: Xgeva®® should drive revenue faster than Prolia®,® it generates up to 13 doses at $1,650 versus 2 at $825 per patient

Source basis: case estimate of 380K potential bone metastases patients; 238K not treated with Zometa®.

Xgeva® carries about two thirds of revenue

The model reaches about $2.12B U.S. revenue by 2015, with growth driven mostly by Xgeva® while Prolia® builds more gradually.





Revenue grows from $1.28B to $2.12B

Unit demand reaches 1.71M injections in 2015

$5.16B

3-year total revenue

Across Prolia® and Xgeva® combined

~67%

Xgeva® revenue mix

+64.7%

Total revenue growth (cummulative)

2013 to 2015 forecast window

Pricing assumptions: Prolia® $825/injection; Xgeva® $1,650/dose.

Xgeva® adoption swings 2015 revenue between $1.55B and $2.76B

Drug prices stay fixed.

WORST CASE

$1.55B 2015 revenue

1.26M injections

Adoption -20%
Lower Persistence/utilization
Shorter Treatment

BASE CASE

$2.12B 2015 revenue

1.71M injections

Current Excel forecast
Most likely projection

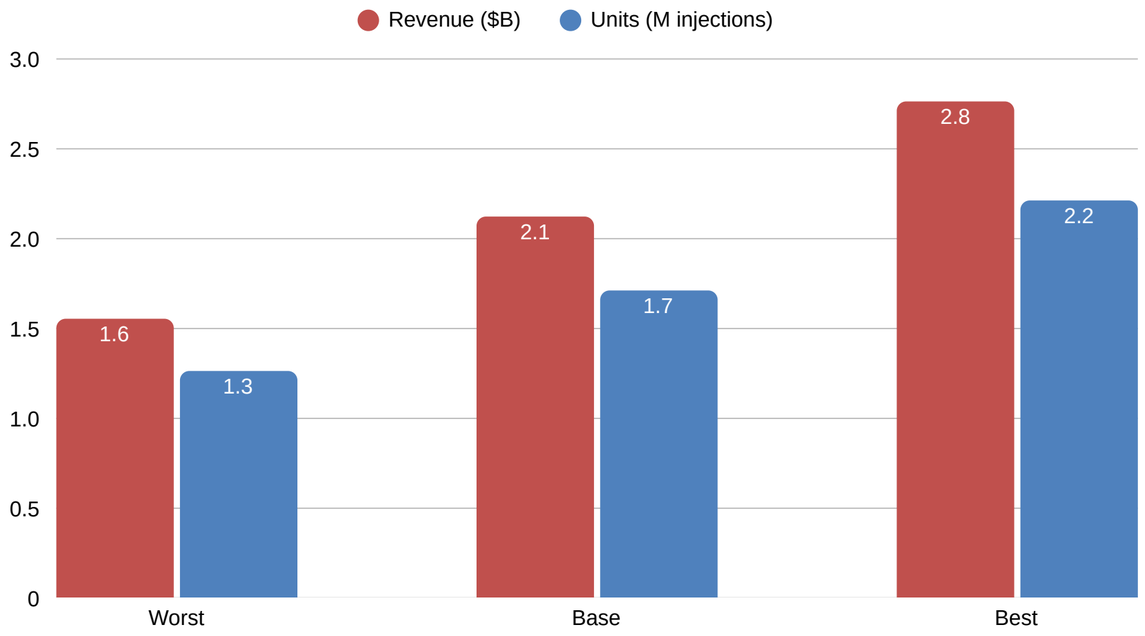
BEST CASE

$2.76B 2015 revenue

2.21M injections

Adoption +20%
Persistence/utilization higher
Longer Treatment

2015 revenue and units under three scenarios



Xgeva® adoption is the largest swing factor because each patient generates more annual units and revenue than Prolia®.

Xgeva® adoption ±20% moves 172,000 units and $284M.

Prolia® adoption ±20% moves 170,000 units and $140M

Recommended interpretation:

plan around the base case, but monitor Xgeva® first; it determines whether 2015 revenue lands closer to $1.55B or $2.76B.

Recommendation: plan to $2.1B in 2015

Base case is $2.1B of U.S. revenue in 2015 on 1.71M injections. About two thirds is Xgeva®.

- *Prioritize Xgeva while building Prolia through targeted adoption*

Where it Wins

Both markets have large untreated pools, not new patients. 238,000 of 380,000 bone metastases patients get no SRE therapy (p. 10), and Amgen estimates half of osteoporosis patients get nothing (p. 8). Xgeva® beat Zometa® on time to first SRE in both breast and prostate trials (p. 10), and oncologists already run buy-and-bill inventory (p. 11).

Where It Could Falter

Prolia® fights a $650 generic that holds 53% of scripts , and Reclast, the only other injectable, never passed 8%. Primary care doesn't stock inventory. Zometa® goes generic in 2013 right as Xgeva® asks for 2x the price.

Watching point

Xgeva® adoption it has about the same number of units as Prolia® but twice the revenue, $284M against $140M.

	Prolia®	Xgeva®
Patients	460K	89k
Injections	850K	862K
Revenue	$701M	$1,422M

Citations

1. Amgen Inc. (2011, January 24). Amgen's fourth quarter 2010 adjusted earnings per share increased 11 percent to $1.17; full year 2010 adjusted earnings per share increased 6 percent to $5.21 [Press release].
2. Calkins, T., & Aggarwal, N. (2011). Forecasting denosumab (Case No. KEL531). Kellogg School of Management, Northwestern University.
3. ChatGPT was used to review calculations, check for inconsistencies or contradictions across the Excel model and presentation, and provide feedback on clarity and organization. All final analysis and decisions were my own (https://chatgpt.com/share/6a94d920-7760-83e8-913e-988e7b1b1484)
4. Mendelow, A. L.
5. Porter, M. E. (2008). The five competitive forces that shape strategy. Harvard Business Review, 86(1), 78–93.