FRESH prespective

Conference Presentation

2017 PMSA - Aiken Rosenblatt
FDA Designations

Impact of FDA Special Designations on Sales Performance & the Commercial Environment

Foster Rosenblatt

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Impact of FDA Special Designations on Sales Performance & the Commercial Environment

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Disclaimer II (Data & Methods)

- Industry entities are, with increasing frequency, obtaining and using data sets for marketing research and drug development.

- This presentation discusses potential approaches to estimating post-launch drug sales performance. The ideas presented, although validated empirically, are speculative and should not be construed as industry standard methodologies.

- Each industry entity should have its own internal processes for reviewing the derivation of data and the appropriate and allowed uses of data sets obtained.

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Disclaimer III (Privacy)

- Use of patient-level personal information and physician-level sales or demographic data for commercial analysis may be prohibited by privacy laws in some countries.

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Background of our work

- The U.S. FDA and Congress have, over time, attempted to speed up the regulatory pathway for therapies that are the first available treatments for specific disease states, or have potential to materially improve the standard of care for serious conditions
  - 1992: FDA Accelerated Approval Program
  - 1997: FDA Modernization Act created a “fast track” designation
  - 2007: FDA Amendments Act created “priority review”
  - 2012: FDA Safety and Innovation Act (FDASIA) of 2012 created “breakthrough therapy” designation

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Counts of drugs by designation

(through 12/16)

- 60+ drugs have been designated Accelerated Approval
- 70+ drugs have been designated Fast-Track
- 9 Priority Review vouchers have been awarded
- 57 drugs have been given Breakthrough Status as of Dec 2016

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Some of the questions we set out to answer

General

- What types of drugs are obtaining these special designations? Under what conditions?
- Does the developer/manufacturer have an impact on the likelihood of such designation?

Sales Performance

- What is the impact on launch trajectory in the US?
- What is the halo effect of US launch trajectory in ex-US markets?

Structural Commercial Environment

- Do special designation drugs receive preferred formulary status?
- Is there some relationship between designation status and pricing?
- Do these drugs preempt treatment algorithms or guidelines? Do they change the standard of care?
- Are specialty market drugs (e.g., rare diseases, biologics, etc.) more likely to obtain designation than non-specialty?

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Some definitions used in this presentation

Drug

- A compound/formulation combination for which an NDA is submitted to FDA under a unique marketed name

Designated

- Drugs granted "accelerated review" (from 1992), "fast track" (since 1997), "priority review" (since 2007) or Breakthrough (since 2012) status

Non-Designated

- Drugs that ***have not been granted*** "accelerated review," "fast track," "priority review" or Breakthrough status

Designated Pre-2012

- Drugs granted some level of FDA priority designation ***prior to*** the 2012 FDASIA

Designated Post-2012

- Drugs **granted Breakthrough Status** by the FDA under the 2012 FDASIA

Global halo effect

- Market share/trajectory in Europe & APAC of drugs that were granted a designation in the U.S. (we do not assess the effect of European designations)

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Methodological approach

The Data Analysis Plan

- The analysis was conducted using IMS MIDAS Gross Sales and Standardized Unit data for observations in markets with at least one designated drug[1]
- A market is defined as a unique combination of country and molecular class, in which multiple drugs compete
- The therapeutic classes included oncology, immunology, virology, cardiovascular and CNS
- To reduce interaction effects from the implementation of the Medicare Modernization Act (MMA), drugs with at least 6 quarters of data that had launched between 2007 and 2015 were included in the analysis

[1]A compound/formulation combination for which an NDA is submitted under a unique marketed name

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Methodological approach

Data Sources

- The total number of unique drugs[1] in the database, in the US, totaled 606
  - 572 drugs did not achieve an FDA designation
  - 34 had achieved some level of designation
  - Drug launches from 2007 onward were considered for analysis; they were were designated as “pre-2012” or “post-2012”

Analytical Methods

- *Estimation of total value* – Drugs were aggregated by designation status to determine the volume of each designation as a proportion of the total market
- *Estimation of market share* – Drugs were grouped by designation status and averages for each of these groups were calculated for eight quarters since drug launch
- *Logit Regression,* using dollar share as the dependent variable, was used to estimate the proportion market share of a drug

[1]A compound/formulation combination for which an NDA is submitted under a unique marketed name

What did we find…

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Let's consider the differential sales performance of designated drugs globally…

Question: How have designated vs. non-designated drugs performed since 2007?

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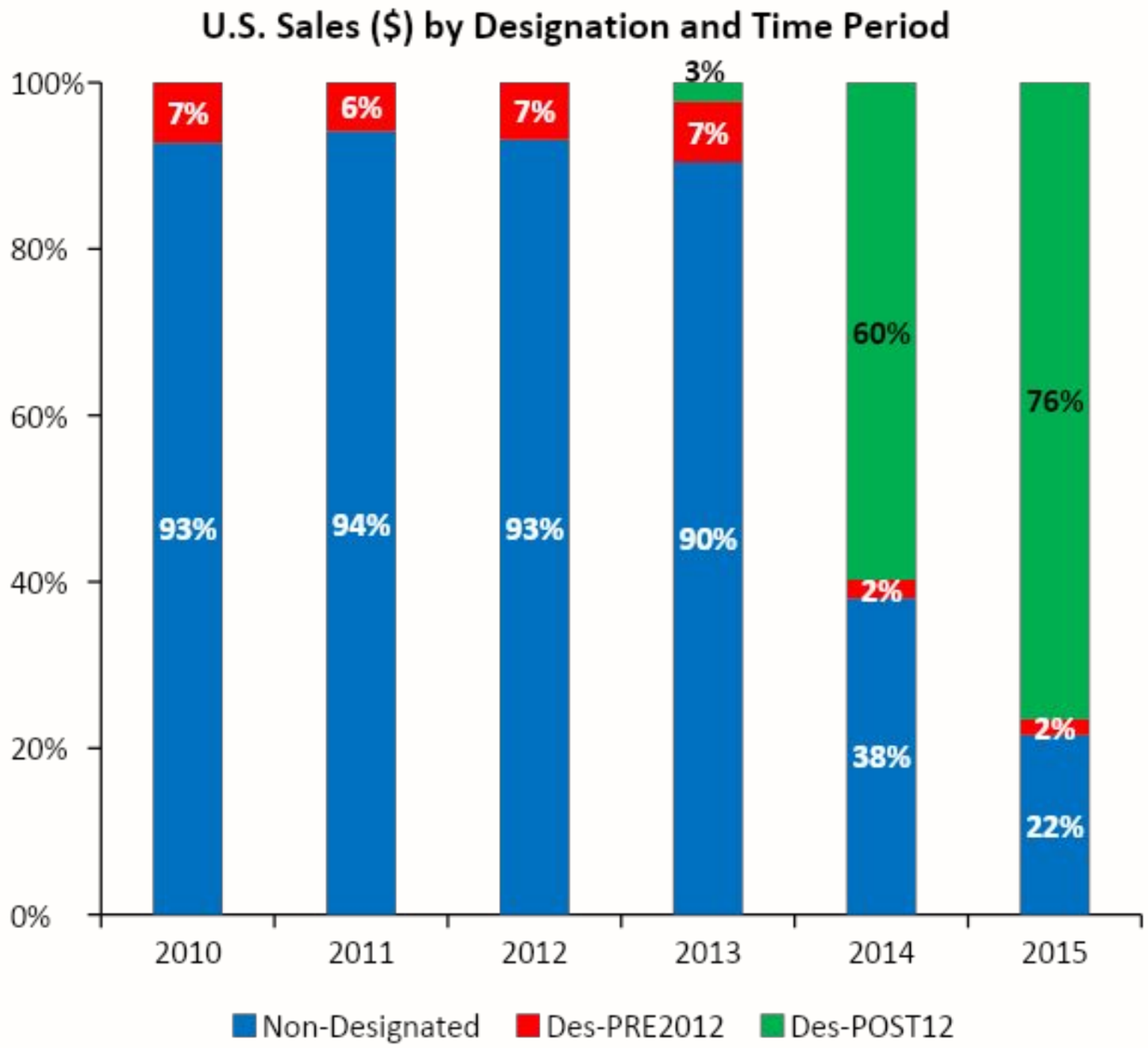
The ***proportionate sales value*** of ***designated drugs*** in the U.S. has been ***steadily increasing*** in markets where they compete

Key Findings

- There has been a significant increase in the proportionate sales value of designated drugs, particularly subsequent to the 2012 Breakthrough Status category
- From 2007 through 2012, drugs that had been designated for some level of priority review accounted for ~7% of sales within their therapeutic classes
- This has changed dramatically since 2012, where drugs designated as Breakthrough Status in 2015 accounted for 76% of sales value within their therapeutic class



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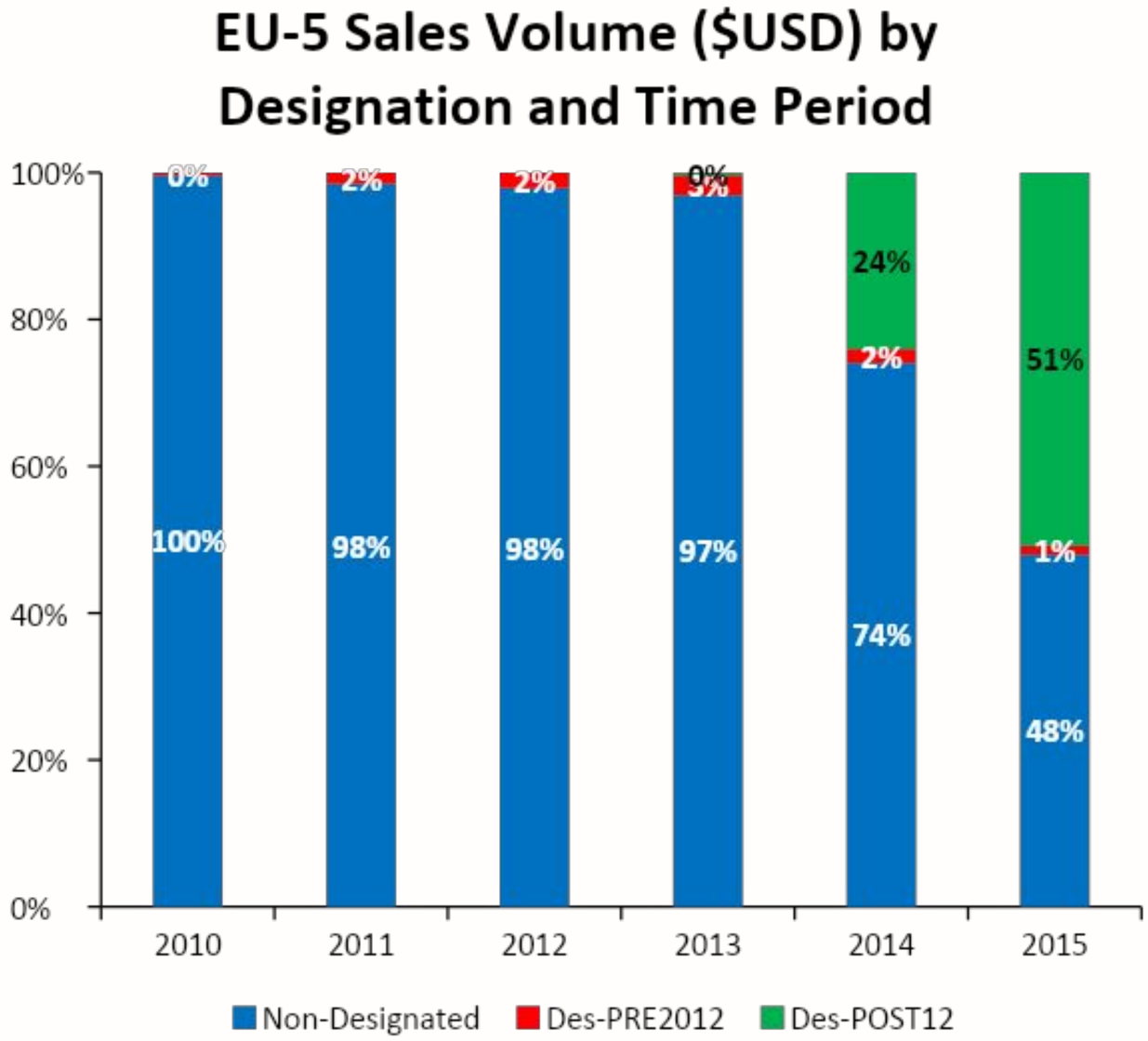
There appears to be a ***sales halo effect*** in the EU-5* for drugs that have been designated in the U.S.

Key Findings

- There has been a significant increase in the proportionate sales value of drugs in the EU-5 that have been granted Breakthrough Status in the U.S.
- From 2007 through 2013, drugs that had been designated for some level of priority review in the U.S. accounted for 2-3% of EU-5 sales share within their therapeutic class
- This has changed dramatically since 2013, where drugs designated Breakthrough Status in the U.S. accounted for 51% of EU-5 sales share within their therapeutic class



** A similar halo effect is seen for European countries as a whole*

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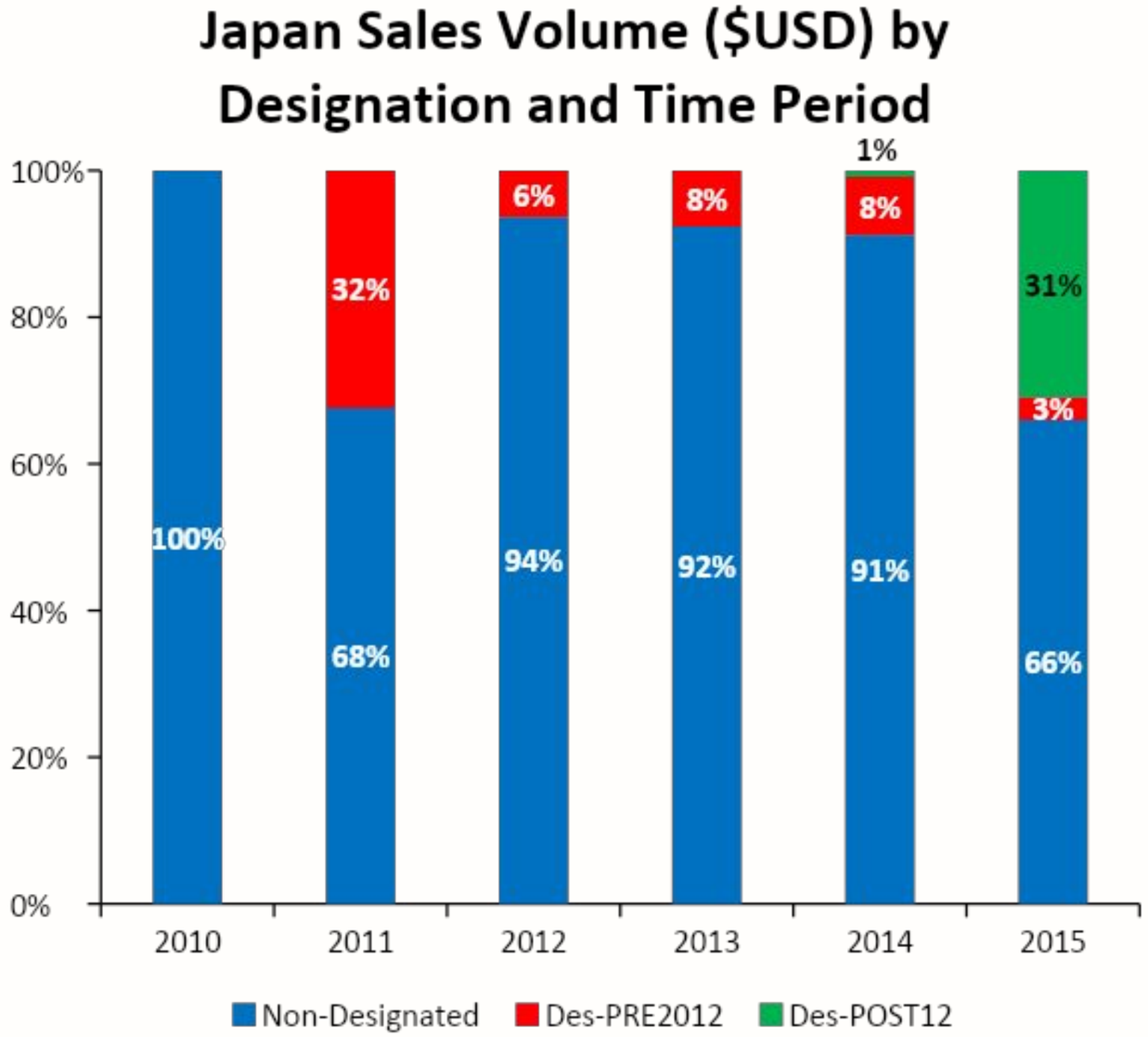
There is, to a ***lesser extent***, a ***sales halo effect*** in Japan for drugs that have been designated in the U.S.

Key Findings

- In 2011, drugs that had been designated in the U.S. for priority review accounted for 32% of the sales value in Japan, in markets within which they competed
- This dropped in 2012-2014, potentially due to implementation of price regulations in Japan
- By 2015, drugs designated as Breakthrough Status in the U.S. accounted once again accounted for 31% of Japanese sales value in markets where they compete



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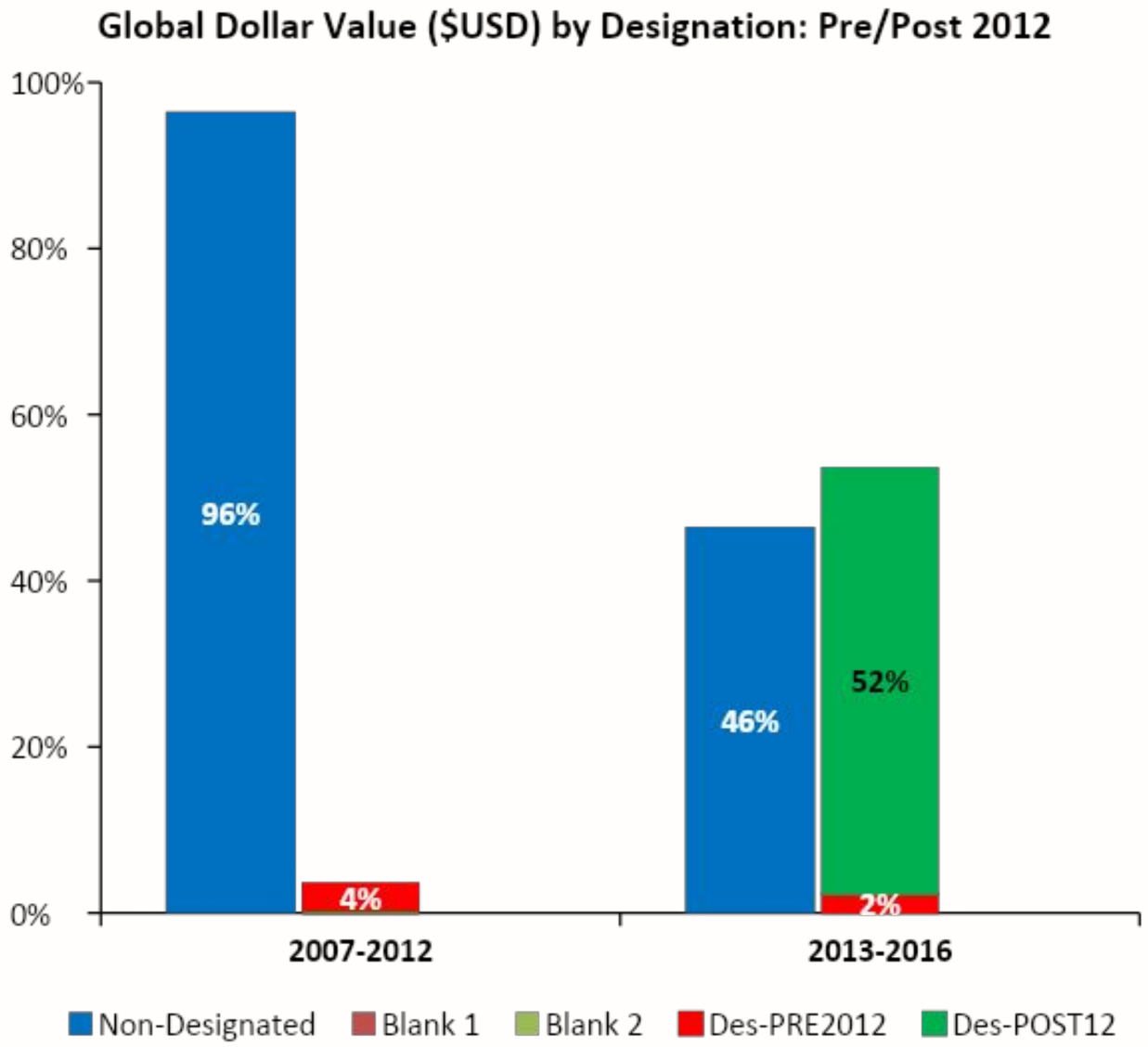
The impact of the 2012 FDASIA designations, appears to have had a dramatic impact on the sales of drugs on a ***global basis***

Key Findings

- Globally, ***prior to the 2012*** Breakthrough Status category, drugs that had been granted some level of priority review in the U.S. accounted for ***4-5% of global sales*** in markets in which they competed
- After enactment of the 2012 FDASIA, **between 2013-2016**, drugs granted Breakthrough Status accounted for ***52% of global sales*** in markets within which they competed



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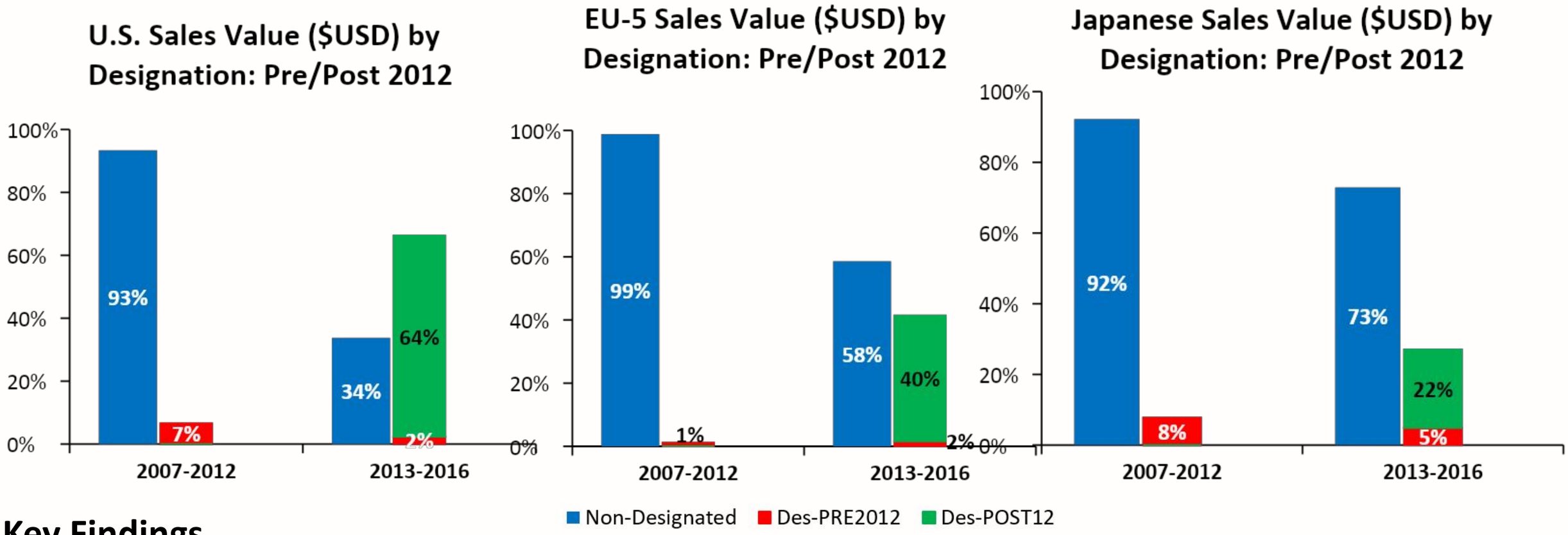
The share lift for breakthrough therapies is most evident in the U.S. (64%) followed by EU-5 (40%) and Japan (22%)



Key Findings

- There has been a global impact of the FDA 2012 Breakthrough Status designations
- The greatest market share effect not surprisingly is in the U.S., where drugs granted Breakthrough Status based on the 2012 designations, now have 64% of market share

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Let’s review the impact of designations on sales trajectory and market share…

Question: To what extent might the designations granted by the U.S. FDA have this effect, incremental to the rapid uptake expected for a new therapy for a condition with high unmet need?

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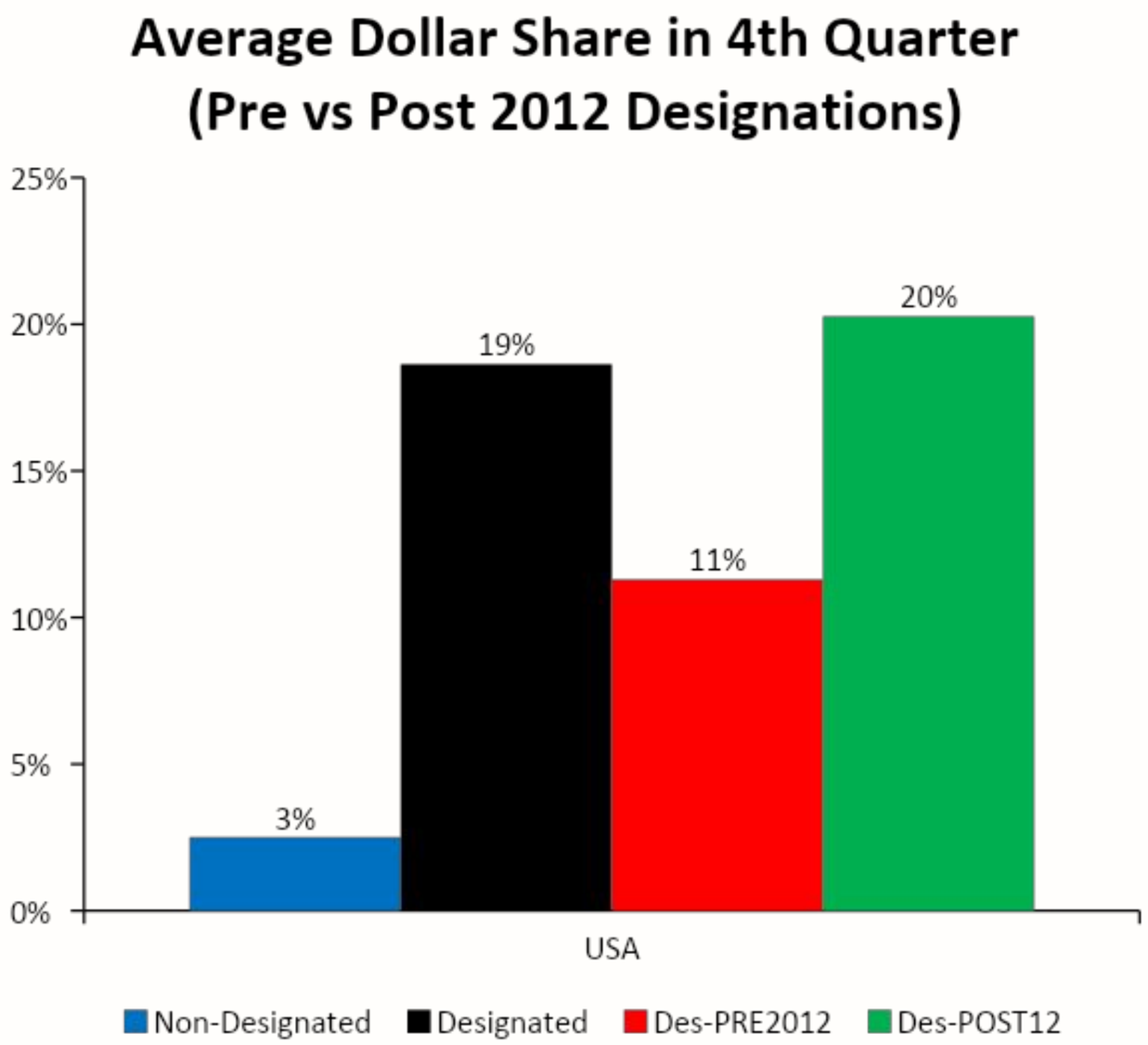
Clearly, a pattern exists, with ***designated drugs outperforming*** non-designated drugs in the U.S.

Key Findings

- There is a statistically significant difference (p<.001) in sales share ***after 4 quarters*** between designated drugs (19%) vs. non-designated (3%)
- The difference is significant for non-designated drugs (3%) vs. drugs designated prior to 2012 (11%) as well as those designated post-2012 (20%)
- Drugs granted Breakthrough Status post-2012 achieve ***twice the sales share*** (20% vs 11%) versus pre-2012 designated drugs after 4 quarters



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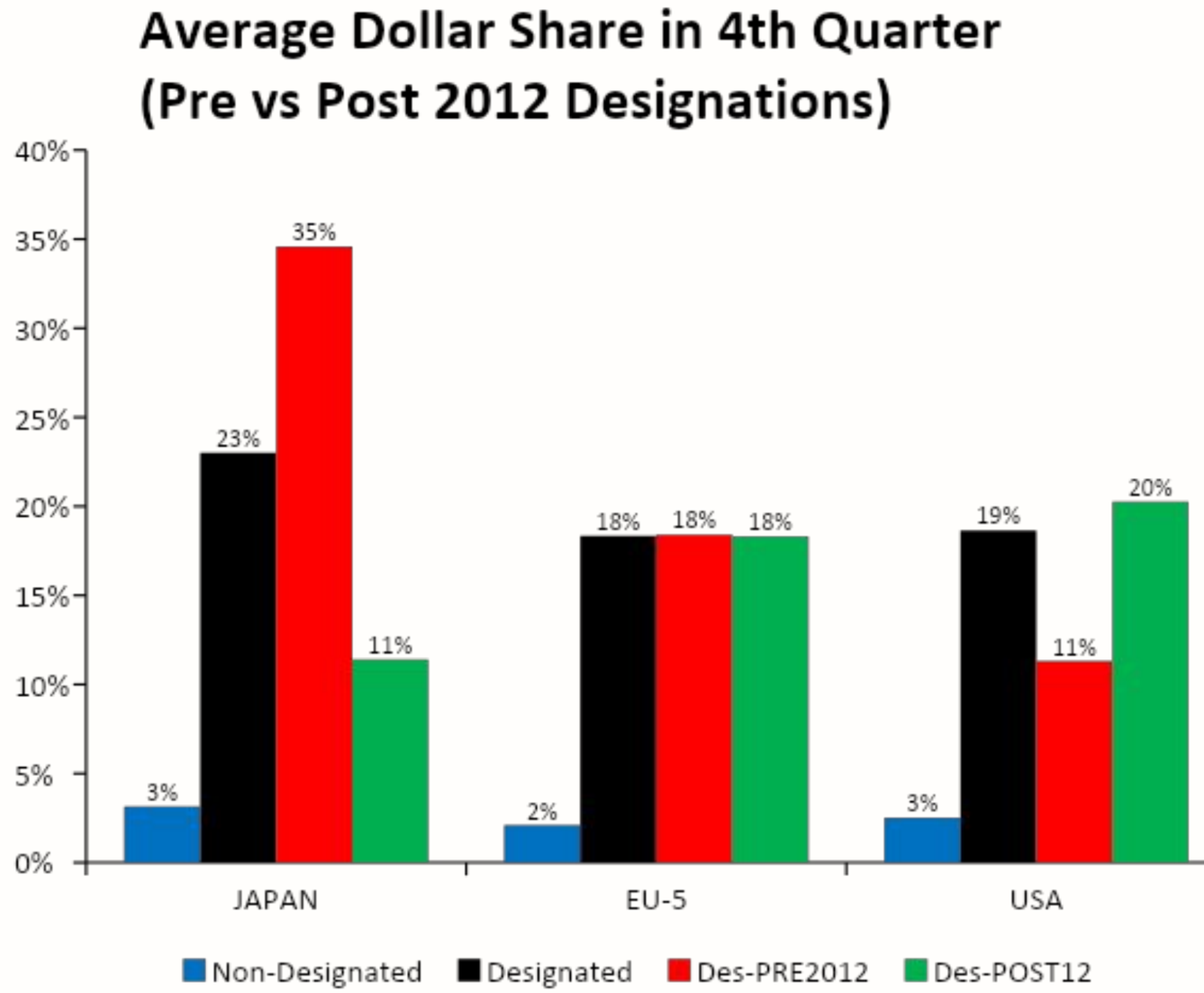
There appears to be a ***halo effect*** in EU-5 and Japan for drugs that have received a U.S. designation

Key Findings

- Overall in Europe, there is a statistically significant difference in sales share after 4 quarters between drugs that were granted some level of U.S. designation (18%) versus those receiving no designation (2%)
- Overall in Japan, the results are similar (23% vs 3%)
- In Europe, post-2012 designated drugs achieved roughly equivalent share compared to pre-2012 (18%)
- In Japan, post-2012 designated drugs achieved lower share than pre-2012 (11% vs 35%)



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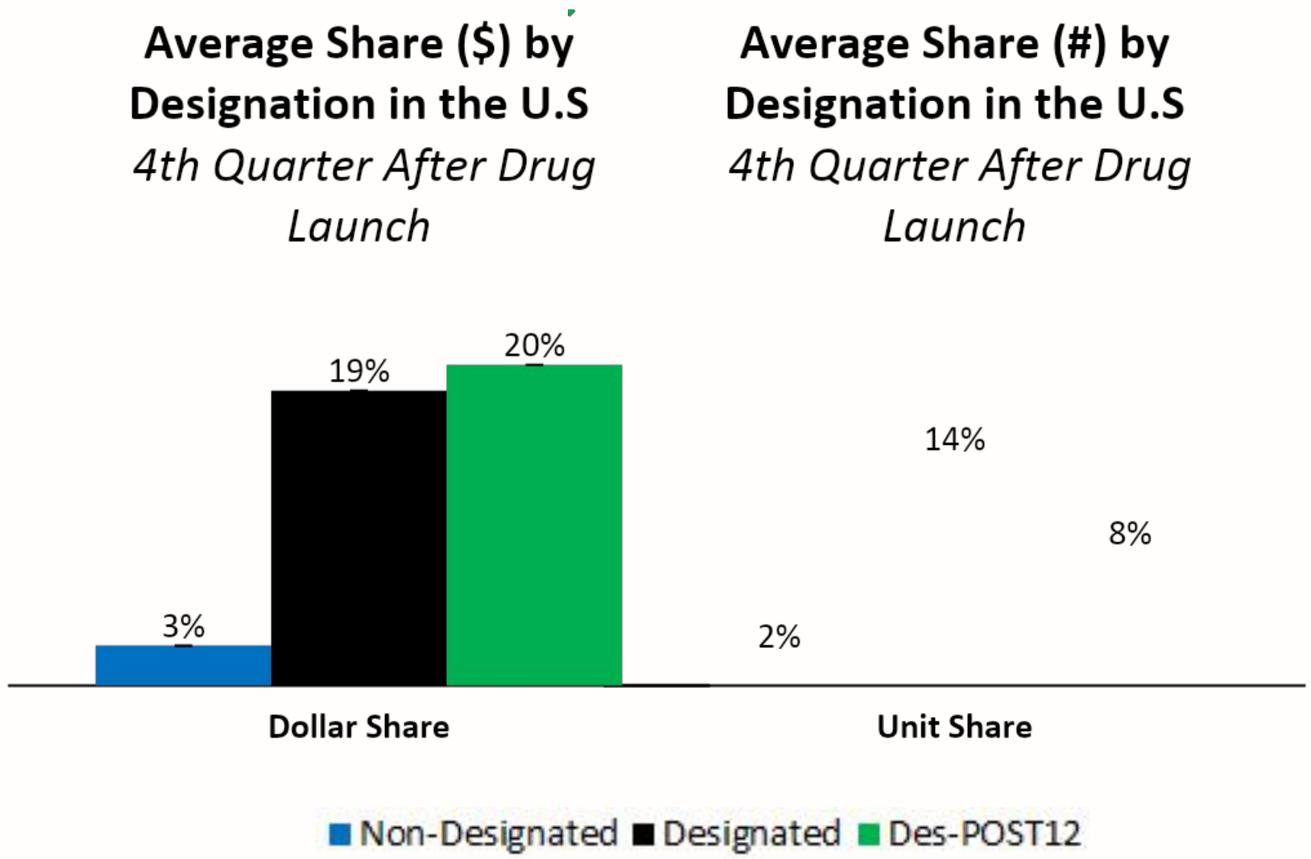
For all designated drugs, there is a ***price premium*** over non-designated drugs; this is especially true for post-2012 drugs

Key Findings

- *For non-designated drugs*, the ratio of sales share (3%) to unit share (2%) has been consistent during the 2007 to 2016 time frame
- However, the ratio of sales share for designated drugs changed with the 2012 introduction of Breakthrough Status
  - Pre-2012 the ratio of sales share to unit share for designated drugs was (19%/14%) or 1.36
  - Post 2012, the ratio was 2.5 (20%/8%)
  - This implies that the post-2012 designated drugs achieved higher sales share ***due to higher relative price***



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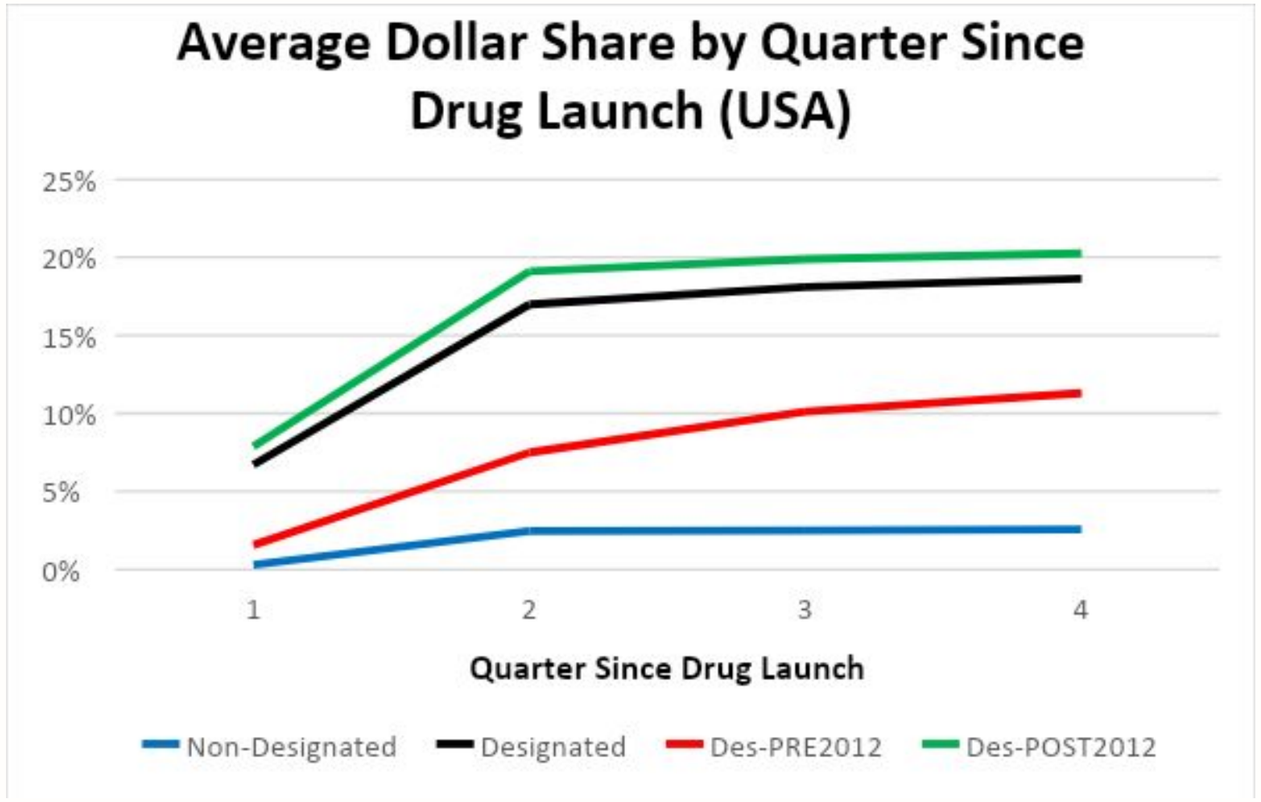
In the U.S., designated drugs have a much faster share uptake compared to non-designated drugs

Key Findings

- In general, share trajectory and share attainment by the 4th quarter of designated drugs (19%) is much faster and steeper relative to non-designated drugs (3%)

- Drugs granted Breakthrough Status (20%) post 2012 achieved nearly twice the sales share by the 4th quarter after launch compared to drugs granted Fast-Track Approval pre 2012 (11%)



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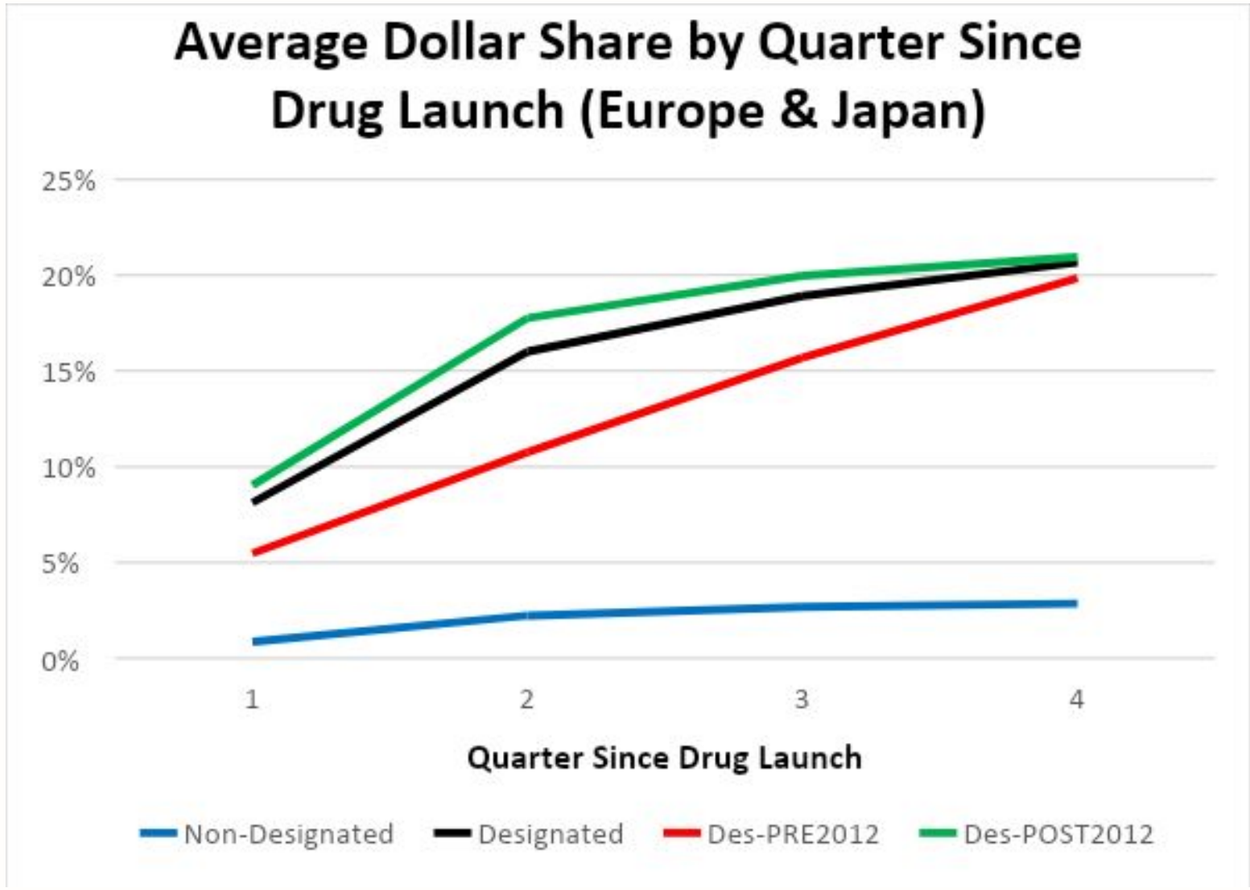
Again, there appears to be a halo effect in Europe and APAC for drugs that have received a U.S. designation

Key Findings

- In general, the share trajectory and share attainment by the 4th quarter of "designated" drugs (20%) is much faster and steeper relative to "non-designated" drugs (3%)

- While the overall 4th quarter sales share is relatively consistent between pre- and post-2012 designated drugs, those granted Breakthrough Status exhibited a convex trajectory, while the pre-2012 designated drugs exhibited a relatively linear growth trajectory



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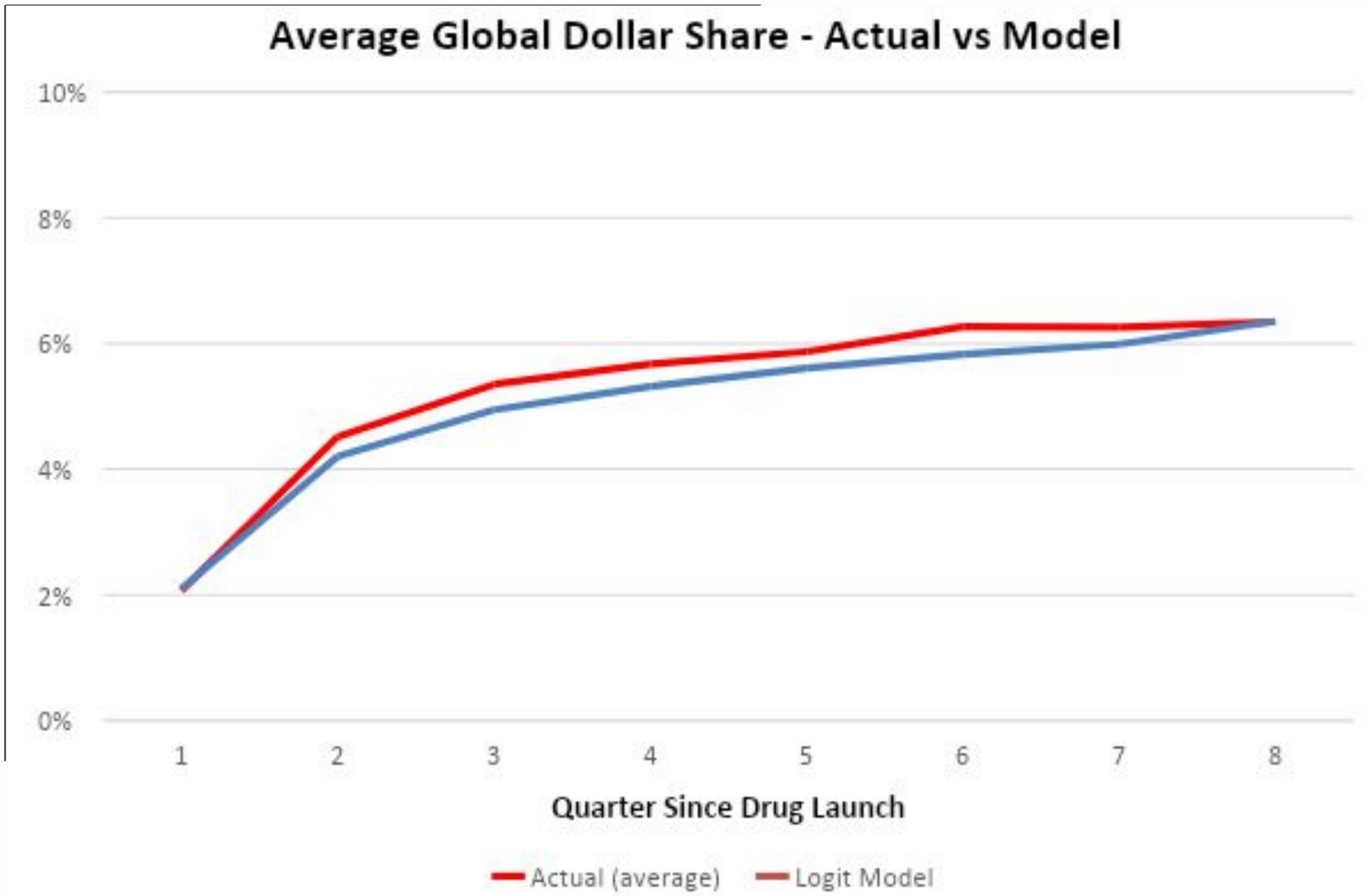
Overall, designation status appears to be a strong predictor of market share*

Key Findings

- On a global basis, there is a strong relationship between the calibrated regression model and share attainment for the first 8 quarters of sales

- The results are consistent across countries, but do vary between therapeutic classes



** For all models the independent variables including order of entry, company size (within a TC by country, and designation status (yes/no) were statistically significant (p<001)*

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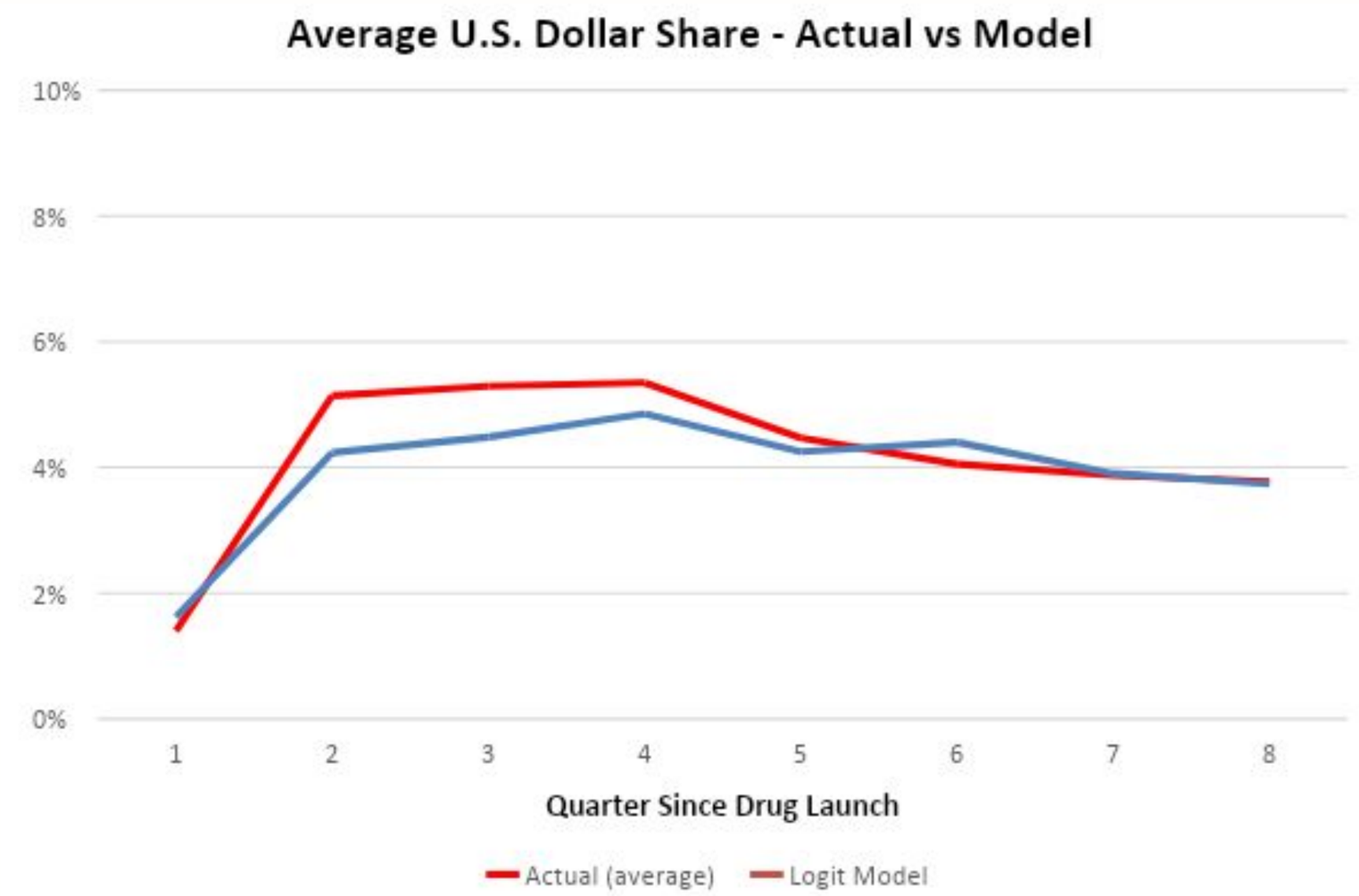
In the U.S, designation status also indicates a higher post-launch dollar share*

Key Findings

- For the U.S. markets, there is a strong relationship between the calibrated regression model and share attainment for the first 8 quarters of sales
- The resulting model is generally predictive, but there is some variability between therapeutic classes
- In 2015-2016, the % of commercial plans listing a product as having “preferred status” was highest for drugs designated pre-2012 and lowest for Breakthrough Status drugs



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** For all models the independent variables including order of entry, company size (within a TC by country, and designation status (yes/no) were statistically significant (p<001)*

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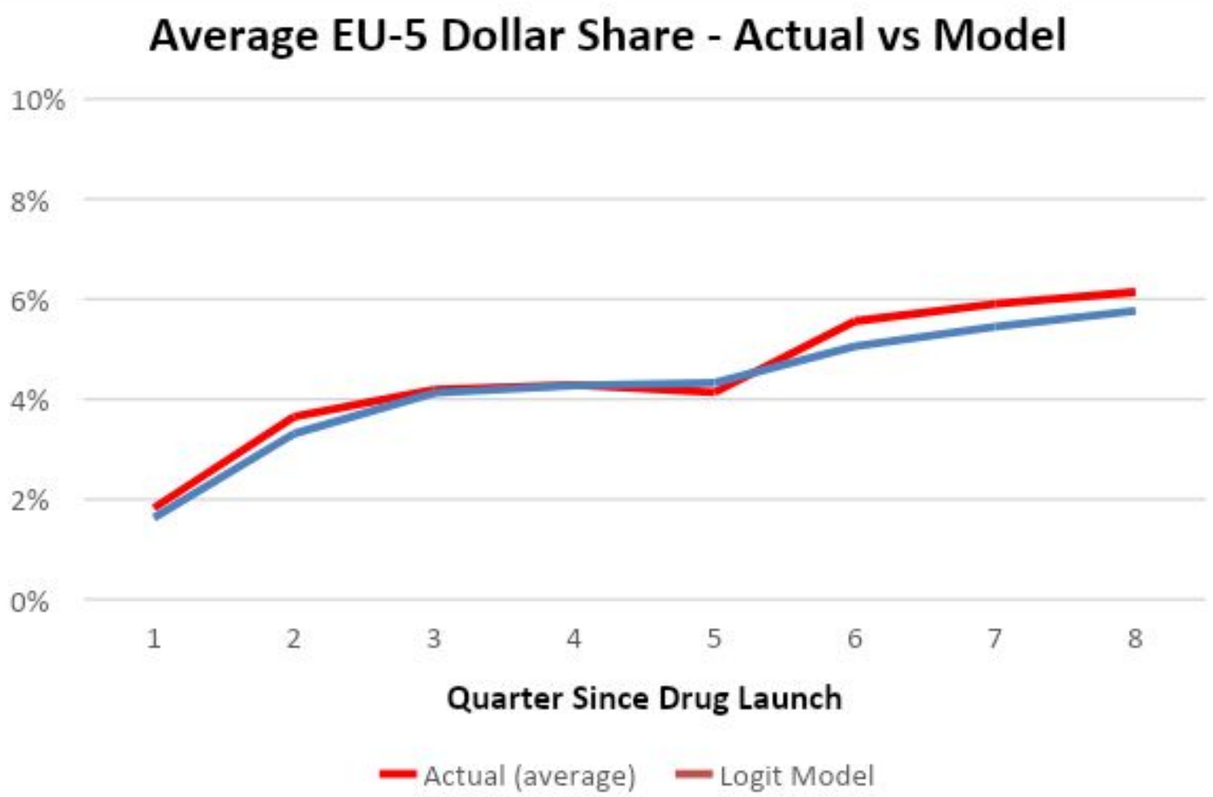
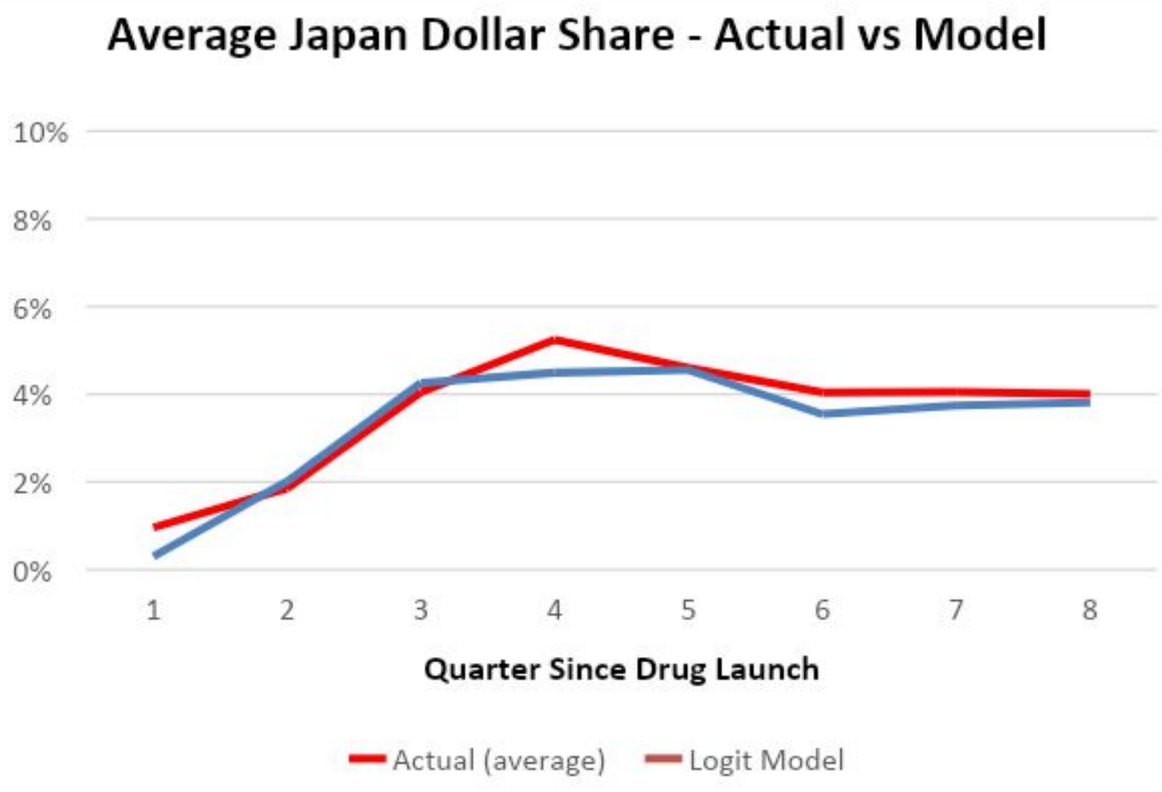
The results for EU-5 and Japan are similar to the U.S. – market share in the first 4-8 quarters are correlated to designation status





- The results for EU-5 and Japan are consistent with the results of the U.S. markets

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** For all models the independent variables including order of entry, company size (within a TC by country, and designation status (yes/no) were statistically significant (p<001)*

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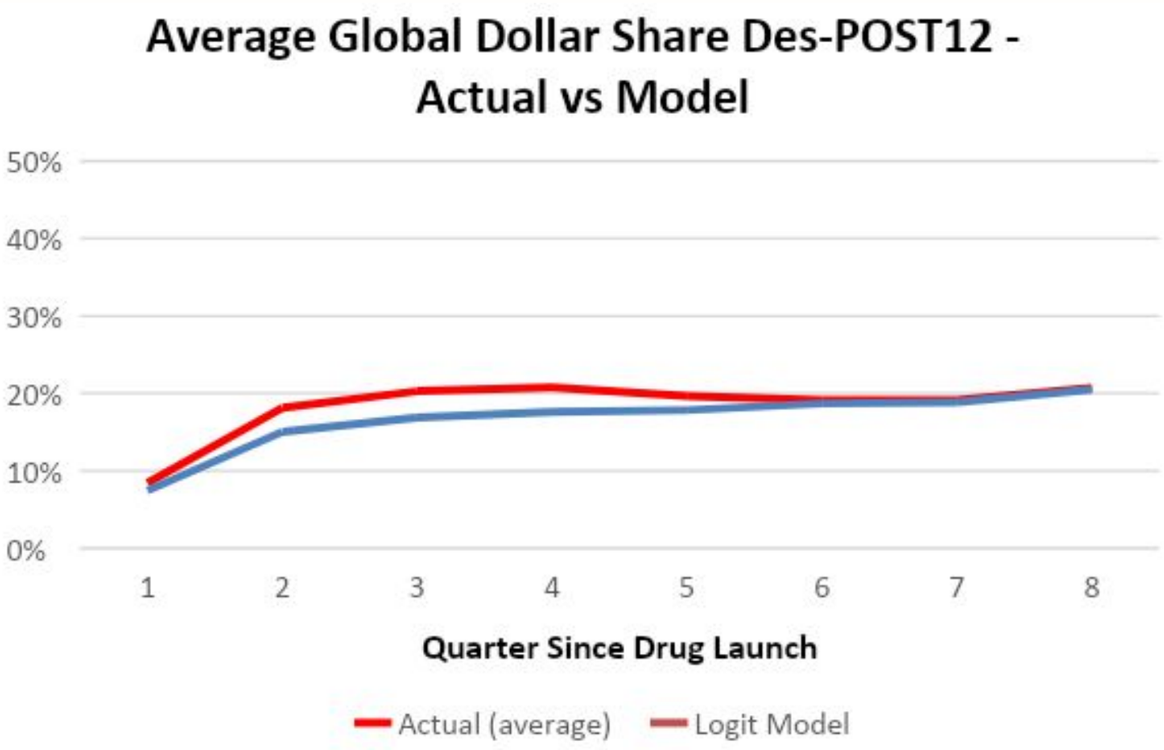
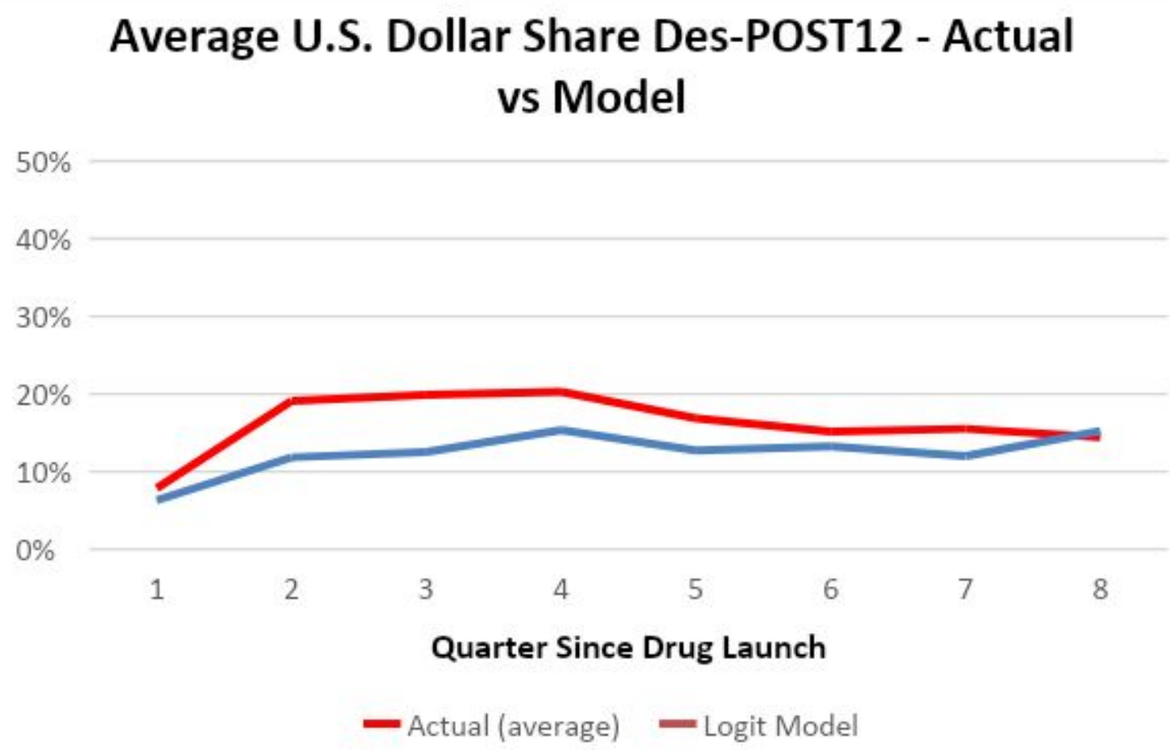
Specifically, Breakthrough Status (post-2012 designation) appears to be a strong predictor of market share





Key Findings

- All model results (for all regions) show a statistically significant result for Breakthrough Status as a predictor of market share over the first 8 quarters

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** For all models the independent variables including order of entry, company size (within a TC by country, and designation status (yes/no) were statistically significant (p<001)*

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Summary & Conclusion

Synthesis, implications, and further research

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Summary of Findings

- ***Overall, the impact of the 2012 FDASIA Breakthrough Status designation appears to have had a dramatic impact on the sales of drugs on a global basis, more so than earlier "priority approval" designations***
- The proportionate sales value of designated drugs versus non-designated drugs in the U.S. has been steadily increasing in markets where they compete; the impact is across multiple broad therapeutic categories
- There appears to be a sales halo effect in the EU-5 and Japan for drugs that have been designated in the U.S.
- Designated drugs strongly outperform non-designated drugs in the U.S. in terms of 1st and 2nd year market share; this is also true for the EU-5 and Japan
- Between 2015-2016, the % of commercial plans listing a product as having "preferred status" was highest for drugs designated pre-2012 and lowest for Breakthrough Status drugs

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Where do we go from here?

Future & Expanded Research

- More detailed investigation into the following:
  - Impact of designation status by specific therapeutic classes by region
  - Use of additional data to validate certain hypotheses (e.g. claims data to identify usage by tumor type for Oncology drugs; primary market research with physicians; independent product valuation assessments (e.g. France ASMR rating) as an independent variable)
- There is a significant price premium for designated over non-designated drugs; however, preferred access is not necessarily improved with a designation; we recommend further investigation into formulary impact of designation status
- Pricing implications of designation status
- More detailed qualitative & statistical analysis constructing a causal model, to address the “800 pound gorilla” in the room…
  - ***Do products that are designated as “breakthrough” achieve faster and greater sales success simply because they are better, or does the designation provide an incremental lift?***

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