TRINITY

WHITE PAPER

Cracking the Code of the Access Landscape in China

Analysis of the 2021 NRDL Update

Rya Zhang • Flora Chung • Yitong Li • Wenting Zhang • Maximilian Hunt

November 2022

Executive Summary

» The success rate of the 2021 National Reimbursement Drug List (NRDL) negotiation hit a historic high since 2019, reinforcing the NRDL as the major access pathway for new therapies in China.

» Concerned about budget impact and sustainability, Chinese payers expect steep price reduction for innovative therapies to reach the potential informal price cap: RMB 300K / USD 41K for oncology and rare diseases, RMB 12K / USD 1.6K for prevalent chronic conditions.

» While the price reduction may be daunting, NRDL inclusion allows access to large patient volume and unlocks significant commercial opportunity, leading to dramatic revenue growth immediately after the NRDL update.

» Small price premium can be achieved in NRDL negotiation with robust evidence on clinical benefits over current treatment.

Click here to access the on-demand webinar that precedes this white paper **'Dragon's Offer: Imparting Wisdom About Market Access Through the NRDL in China'** (September 2022).

Trinity's Take

As the market becomes increasingly crowded and budget constraints continue in China, downward pricing pressure to secure NRDL listing remains the top challenge for multinational pharma companies in China. However, the significant uptake post-NRDL inclusion and broad access offers substantial opportunities for innovative products with clinical differentiation.

Highlights of the 2021 NRDL Negotiation

- **Recently launched products make up a high proportion of NRDL additions**
- **During NRDL negotiations, branded products experience consistently high price reductions**
- **Post-NRDL listing, products experience sustained revenue growth**

Under the State Council's 'Health China 2030' initiative, the pricing and market access (P&MA) landscape in China has been rapidly evolving with increasing emphasis on a centralized access pathway, better utilization of the public medical insurance fund and greater transparency in the pricing and reimbursement negotiation process. The centerpiece of this changing landscape is the NRDL.

Since its first negotiation in 2017, the NRDL has become the most important market access pathway in China, providing broad coverage, deep penetration and uptake opportunities for listed products. 2021 marked the fifth consecutive year of NRDL negotiation. Despite the lingering impact of COVID-19, the overall negotiation success rate has been steadily climbing since 2019, reaching 80% in 2021. As the public healthcare system in China becomes more mature with each NRDL update, being listed on the NRDL can unlock commercial potential for innovative therapies with significant clinical benefits.

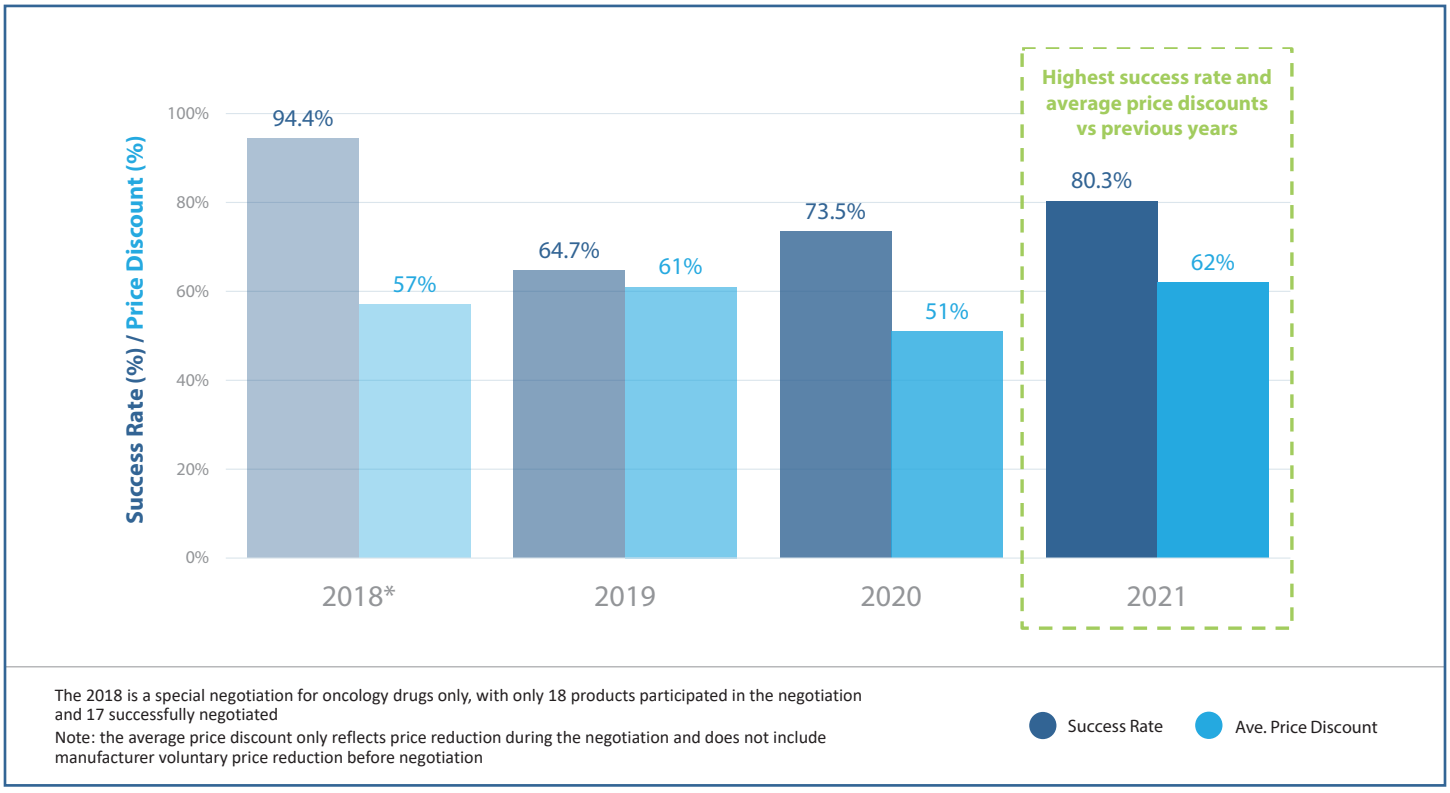


FIGURE 1 | 2018-2021 NRDL Negotiation Success Rates and Pricing Discount (%)

1 Recently Launched Products Make Up a High Proportion of NRDL Additions

One striking difference of the 2021 NRDL update from prior years' updates is the focus on new approvals. The proportion of products that achieved NRDL inclusion in the same year as regulatory approval nearly doubled compared to last year: 40% in 2021 vs 24% in 2020. We also noted increased representation of products approved within five years on the NRDL updates: nearly all new products successfully negotiated in 2021 were approved within the last five years compared to 71% in the 2020 NRDL update.

In previous NRDL negotiations, it typically took innovative products multiple years between regulatory approval and NRDL listing because:

- Products needed to be nominated by clinical experts for negotiation
- Many manufacturers were highly reluctant to discount

The significant increase in new approvals in the 2021 NRDL update mirrors some manufacturers' determination to secure early NRDL listing and their increased willingness to provide a discount. These observations suggest a potential shift of reduced time lag between regulatory approval and NRDL inclusion, reaffirming the opportunity for a fast path to public reimbursement in China.

2 During NRDL Negotiations, Branded Products Experience Consistently High Price Reductions

After the 2021 NRDL negotiation, the 67 newly listed branded products received a ~62% price reduction on average, maintaining the ~60% average price reduction trends since 2018 (Figure 1). These price reductions only reflect the level of discounting that happened during negotiations while the total price reduction in 2021 may be bigger. Some multinational corporations (MNCs) voluntarily reduced prices before the negotiation as a tactic to demonstrate their determination for NRDL success. For example, Janssen reduced DARZALEX's price by 56% prior to NRDL negotiation, and then took an additional 31% reduction during the negotiation to be successfully listed on NRDL.

Once a product enters NRDL, its price becomes public. This may make MNCs concerned about their global pricing given the significant price reduction in China. Currently, no other markets officially reference China's pricing. Manufacturers can also argue the significant volume provided in China that few markets can offer to justify the high discounts. However, manufacturers should be cautious with their global launch sequencing (especially for first launches) as pricing in China may be unofficially considered by certain markets during price negotiations such as South Korea and Taiwan.

3 Post-NRDL Listing, Products Experience Sustained Revenue Growth

While one may suspect the intense price reduction is disruptive for manufacturers, we have observed positive outcomes from successfully listed products.

Consistent with our prior analysis of products listed after the 2017 NRDL update, products successfully listed on NRDL during the 2018-2020 negotiations have exhibited substantial growth in revenues post-negotiation,

with 2-3x increase in the first year post-NRDL compared to pre-NRDL. The average annual sales for newly listed products participated in the 2019 and 2020 NRDL negotiations were doubled post-negotiation (Figure 2). We also observed more robust growth among MNC products than domestic products (Figure 3). The 114 MNC products included in NRDL since 2017 achieved a ~4x increase in peak annual sales compared to pre-NRDL years, while the 108 domestic products had a ~2x increase.

The dramatic sales increase post-NRDL inclusion is primarily driven by immediate increase in patient volume, as NRDL inclusion makes the treatment affordable and accessible to most patients. Considering the broad and prioritized access to hospital formulary associated with NRDL listed products, we expect the revenue growth trends to continue in the future. However, the growth trend may flatten after ~two years as the existing patient pool becomes well penetrated and growth driver shifts to newly diagnosed patients. In addition, listed products will need to undergo price re-negotiation or review every two years, which may also negatively impact sales. This has already been observed in the 17 oncology products listed after the 2018 negotiation, where sales growth starts flattening in 2020. To maintain healthy growth post-NRDL inclusion, manufacturers need to continuously assess key growth drivers and identify opportunities to unlock additional patient populations.

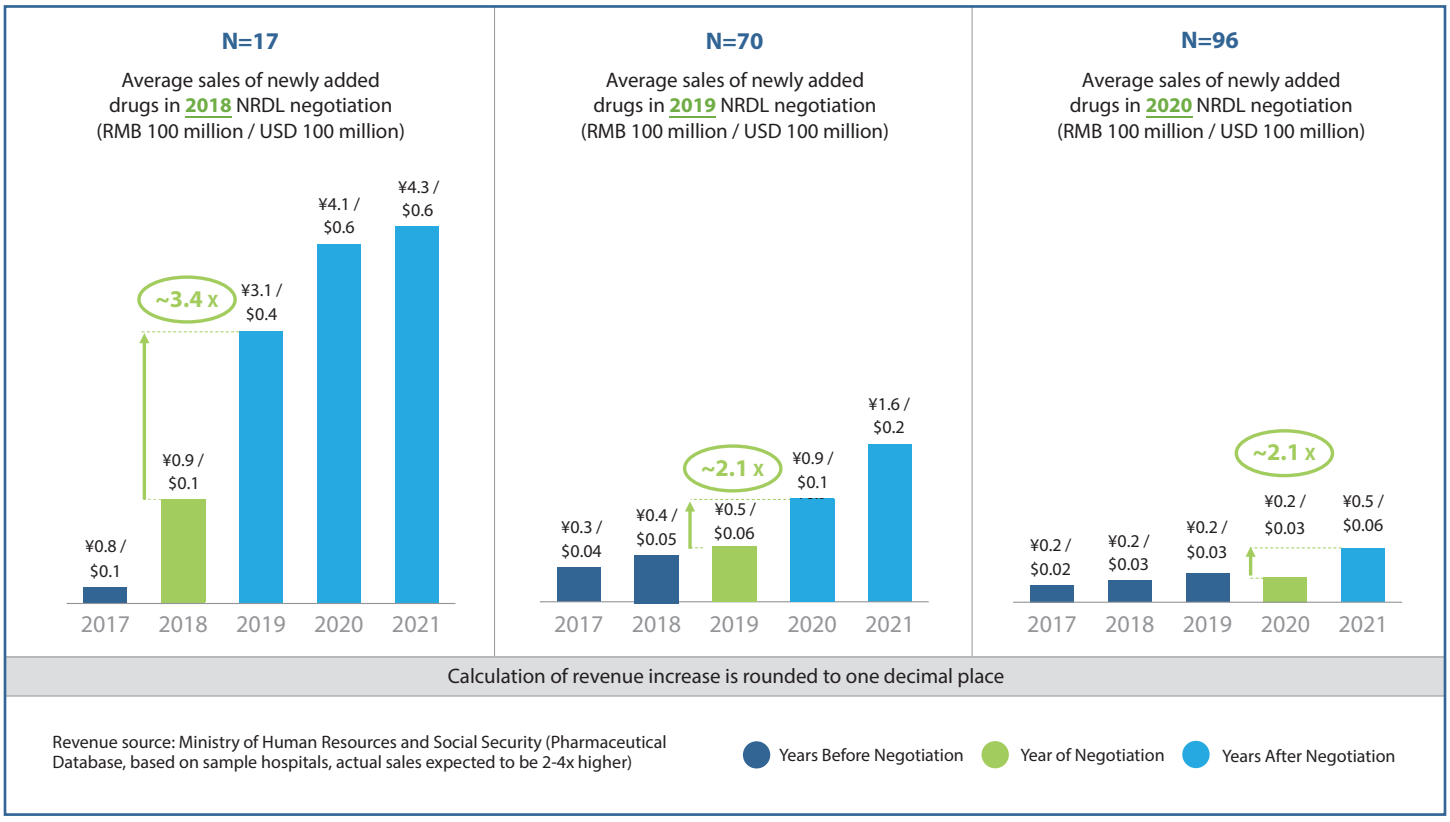


FIGURE 2 | Average Annual Sales of Newly Included Drugs in 2018-2020 NRDL Updates (Pre-NRDL vs Post-NRDL)

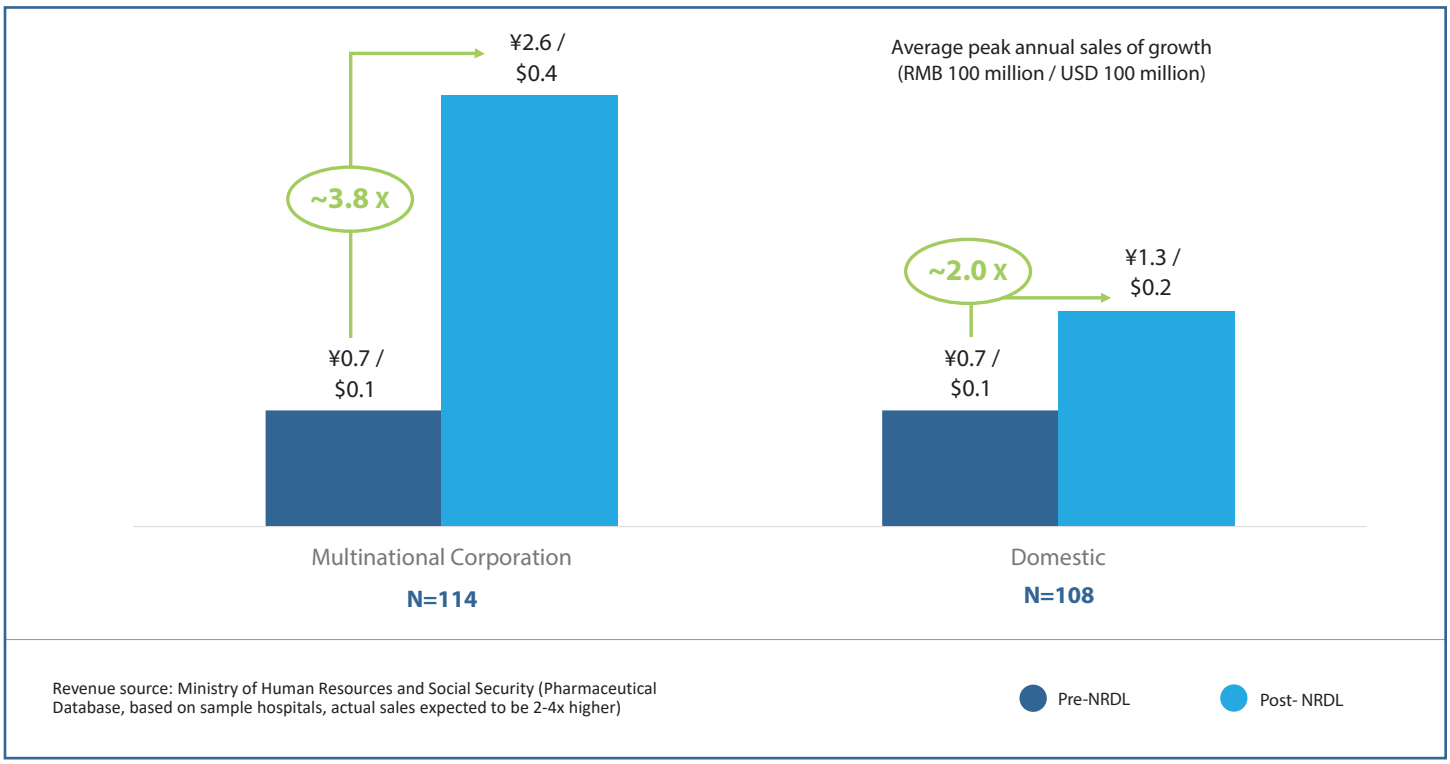


FIGURE 3 | Average Peak Annual Sales Growth of NRDL listed Products from Multinational Corporations vs Domestic Manufacturers

2021 NRDL: Oncology Deep Dive

1 Oncology is Still the Therapeutic Area of Focus

Similar to previous years of NRDL negotiations, oncology remained the priority for NRDL inclusion in 2021. Seventeen innovative cancer therapies were successfully listed on NRDL via negotiation, accounting for 26% of all newly included branded drugs.

FIGURE 4 | Therapeutic Areas of Newly Added Drugs in the 2021 NRDL Update

2 Budget Impact Driven Price Reduction for Oncology Products

Due to budget impact concerns, the National Health Security Administration (NHSA) is determined to control treatment cost and maintain budget sustainability. Annual treatment cost of all newly listed oncology products dropped below or around RMB 300K / USD 41K (Figure 5), implying a potential informal annual price cap for oncology treatment. Products with larger indications received bigger price reduction given consideration on budget sustainability. For example, VIZIMPRO indicated for first line Non-Small Cell Lung Cancer (NSCLC), ERLEADA indicated for prostate cancer and HALAVEN indicated for metastatic breast cancer all reduced price by over 80%, a rate much higher than the rest of the negotiated products.

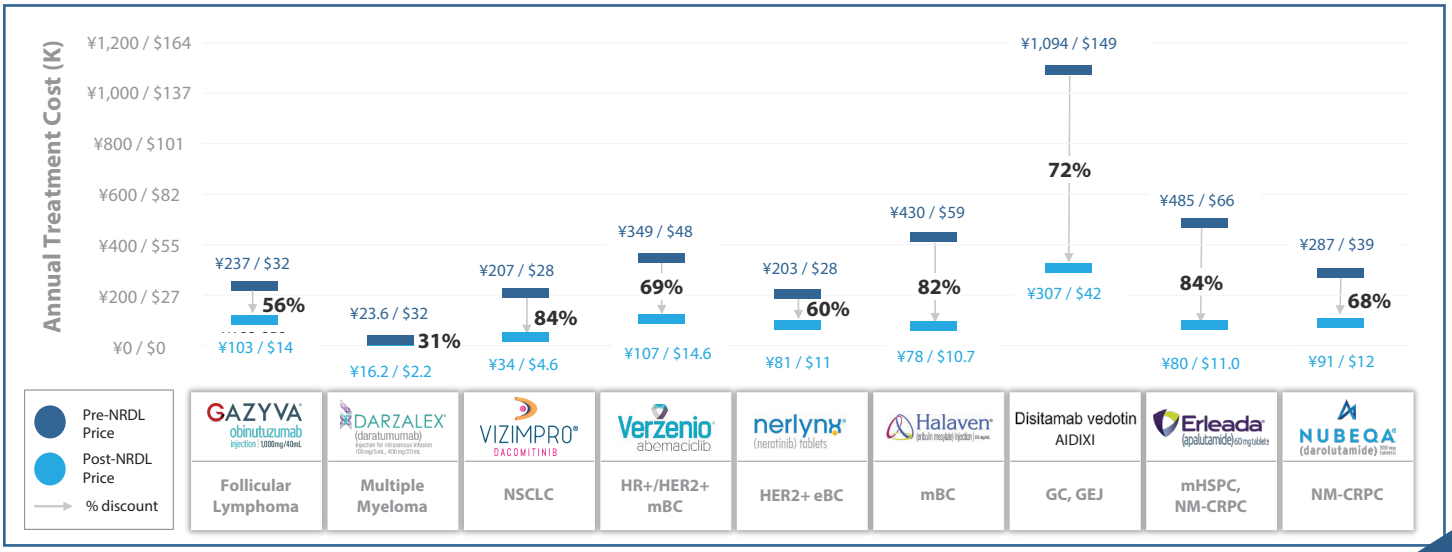


FIGURE 5 | Annual Treatment Costs of 2021 NRDL Additions, Oncology Branded Drugs (K, RMB / K, USD)

3 Indication Expansion of Domestic PD-(L)1s Facing More Payer Scrutiny

Four domestic players occupied China's public reimbursement for check inhibitors via NRDL negotiation. Although steep price reductions are typically observed in therapies treating high-incidence tumors, each check inhibitor's pre-negotiation price and budget impact of indication expansion also play key roles during negotiation. Innovent's sintillimab and BeiGene's tislelizumab both negotiated for the high-incidence NSCLC and hepatocellular carcinoma indications; however, sintilimab received greater price reduction than tislelizumab (62% vs 33%), mainly because sintilimab had a relatively higher starting price due to a small indication prior to the negotiation, and tislelizumab had just been through price-cuts in the 2020 NRDL update to include a urothelial carcinoma indication.

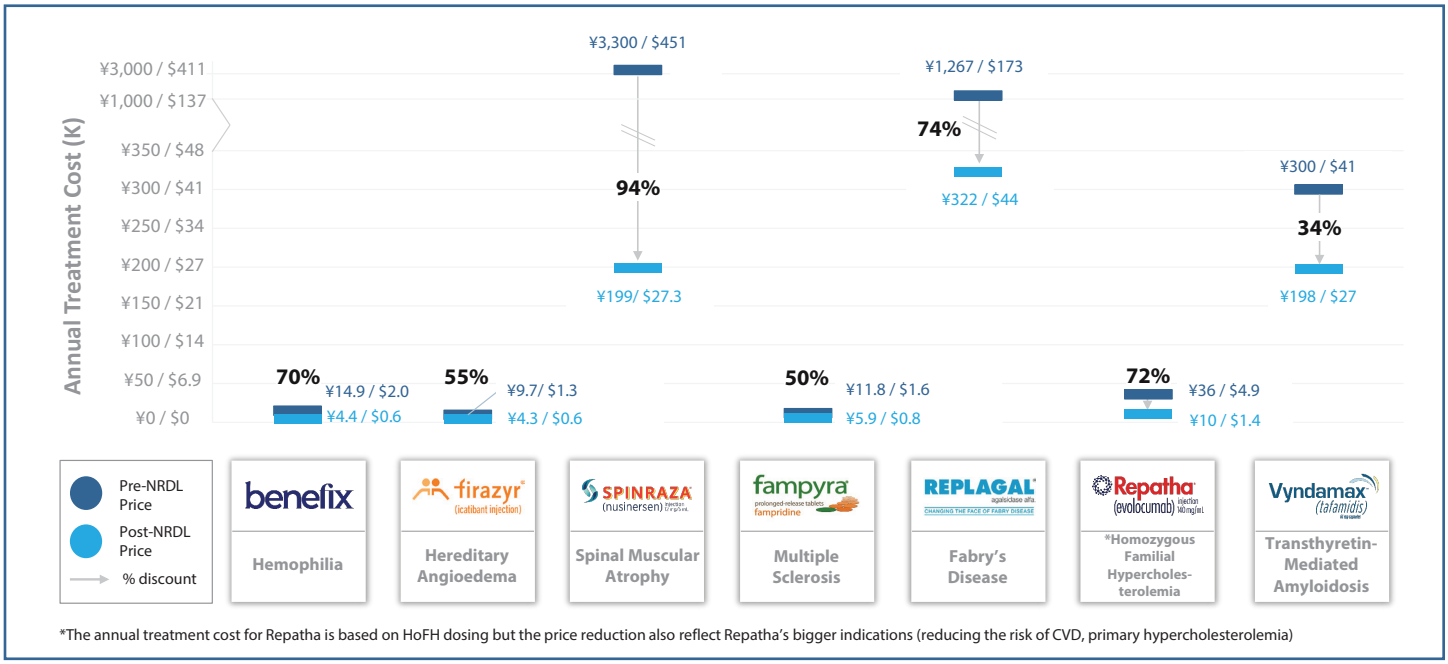
Junshi's toripalimab secured the smallest price-reduction at 9% due to its low starting price (RMB 71K / USD 9.7K) and low-incidence tumor indications (melanoma, nasopharyngeal carcinoma, urothelial carcinoma). In contrast, Hengrui did not offer any price reduction for expanding camrelizumab's indication to nasopharyngeal carcinoma, and thus failed the 2021 NRDL Negotiation. This shows that Chinese payers expect price reduction whenever manufacturers apply for indication expansion, even if the new indication results in a small patient population increase.

4 NRDL Inclusion of MNC PD-(L)1s Becoming More Challenging

Compared to domestic products, NRDL inclusion may be more challenging for MNC PD-(L)1s given fierce competition and cost barriers. Despite Patient Assistance Program (PAP) offers, the average annual treatment cost of MNC PD-(L)1s is still three times higher than that of domestic PD-(L)1s. This cost difference will likely exacerbate as domestic players expand indications and reduce prices in future NRDL negotiations. On the demand side, patients will be less willing to pay for PD-(L)1s not listed on NRDL and instead pursue reimbursed domestic PD-(L)1s. As a result, current MNC PD-(L)1s are forced to seek commercial insurance coverage in the private market.

2021 NRDL: Rare Disease Deep Dive

Rare disease products went through an intense negotiation in 2021; only seven of the 22 candidates that participated in the negotiation were successfully listed. While the same amount of rare disease products were listed after the 2020 and 2021 NRDL negotiations, 2021 rare disease negotiations had a slightly lower success rate (32% vs 34% in 2020) and steeper price reduction (69% % vs 49% in 2020).



*The annual treatment cost for Repatha is based on HoFH dosing but the price reduction also reflect Repatha's bigger indications (reducing the risk of CVD, primary hypercholesterolemia)

FIGURE 6 | Annual Treatment Costs of 2021 NRDL Additions, Rare Disease Branded Drugs (K, RMB / K,USD)

1 High Overall Price Reduction Considering Voluntary Price Reduction

To secure an invitation to the 2021 NRDL negotiation and to increase the likelihood of negotiation success, some manufacturers voluntarily reduced the price of their orphan drugs below RMB 500K / USD 68K prior to the negotiation. For these products, the 'actual' price reduction was greater than the % shown on Figure 6. For example, Pfizer first decreased VYNDAMAX's price by 61.5% in August 2020, and then further reduced it by 34% during the November negotiation, equivalent to a total price reduction of ~74% since launch.

2 No Special Pricing Advantages for Orphan Drugs

Unlike in the U.S. and EU where orphan drugs are allowed a price premium, the RMB 300K / USD 41K informal price cap is still applicable to all innovative therapies in China, including orphan drugs. As one of the most expensive therapies in China, SPINRAZA was priced at RMB 3.3 million / USD 0.5 million per year and did not voluntarily reduce its price prior to the negotiation. However, pressured by the public outcry to cover this life-saving treatment, Chinese payers managed to negotiate SPINRAZA's price down to below RMB 200K / USD 27K per year, achieving a dramatic 94% price reduction. This unprecedented NRDL negotiation success demonstrates Chinese payers' determination to cover innovative life-saving treatment and the orphan drug manufacturers' willingness to discount heavily for broader access.

2021 NRDL: Chronic Disease Deep Dive

Chronic disease therapies are facing higher pricing pressure than oncology and rare disease therapies. We observed that post-negotiation prices for newly listed chronic disease therapies generally fell below RMB 12K / USD 1.6K, much lower than the RMB 300K / USD 41K informal price cap for oncology and rare disease products. This is due to significant patient volume and long-term treatment duration of chronic conditions.

1 Cardiovascular Disease (CVD): Voluntary Price Reduction of PCSK9 Inhibitors

Several MNC candidates that failed in the 2020 NRDL negotiation re-applied in 2021 and were successfully included in the 2021 NRDL update via negotiation, including REPATHA and PRALUENT.

Both PCSK9 inhibitors pursued voluntary price reduction before the negotiation to optimize pricing strategy, with PRALUENT taking a more aggressive price reduction (47% vs 23% for REPATHA, Figure 7). During negotiation, their prices were further reduced by 70% to < RMB 10K / USD 1.4K, resulting in total price reduction of ~80% compared to launch. The final negotiated price of PRALUENT is slightly higher than that of REPATHA. This may be attributable to their difference in indications as REPATHA has an additional rare disease indication of homozygous familial hypercholesterolemia.

Despite significant price reduction, PSCK9s still face challenges in this generic dominant market. Patient co-pay for post-NRDL PCSK9 inhibitors is still higher than that for statin, and statin will likely remain the standard of care.

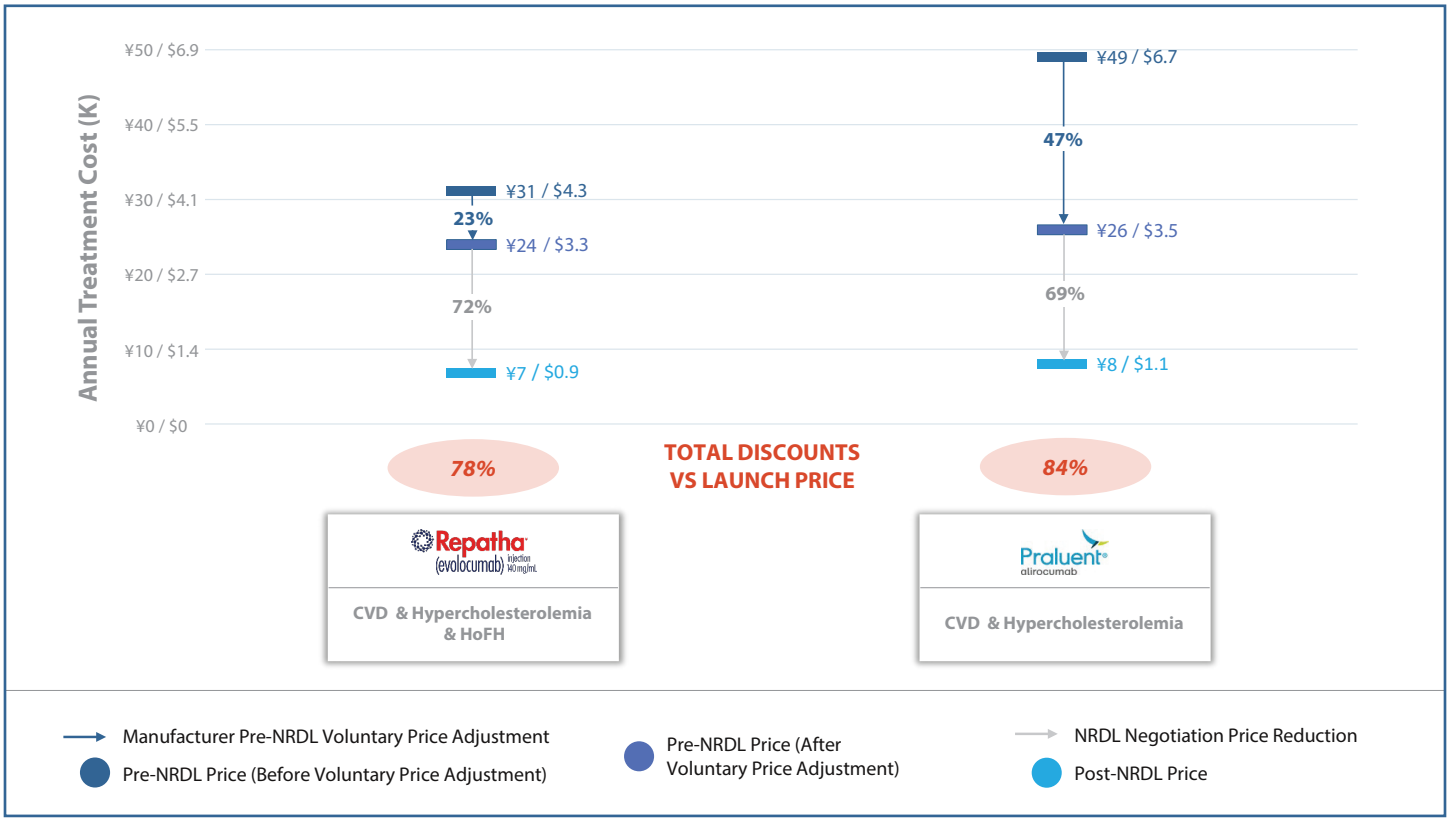


FIGURE 7 | Annual Treatment Costs* of PCSK9 Inhibitors (K, RMB / K, USD)

*Treatment costs are calculated based on the CVD indication dosing

2 Diabetes: Slight Price Premium Achievable With Evidence of Clinical Superiority, While Overall Willingness to Pay for Chronic Therapeutic Areas Remains Low

Seven GLP-1 receptor agonists have been included in NRDL for diabetes over the past few years. Out of these drugs, five are MNC products. Similar to cardiovascular disease, diabetes products generally reduced their price below RMB 12K / USD 1.6K to be listed on NRDL, with the exception of OZEMPIC.

In the 2021 NRDL negotiation, Novo Nordisk's OZEMPIC achieved a premium price and secured the highest post-negotiation annual cost compared to its in-class branded competitors (RMB 12K / USD 1.7K vs ~RMB 8K / USD 1.1K). OZEMPIC demonstrated superior efficacy over standard-of-care in several head-to-head studies, including comparison with DDP-IV inhibitor (sitagliptin), insulin and other GLP-1 products (exenatide & dulaglutide). OZEMPIC's robust evidence on clinical superiority likely justified the premium price during the negotiation, suggesting that Chinese payers are willing to pay a small premium for products with robust clinical profiles. However, given concerns on budget sustainability, the overall willingness to pay for chronic disease therapies remains low.

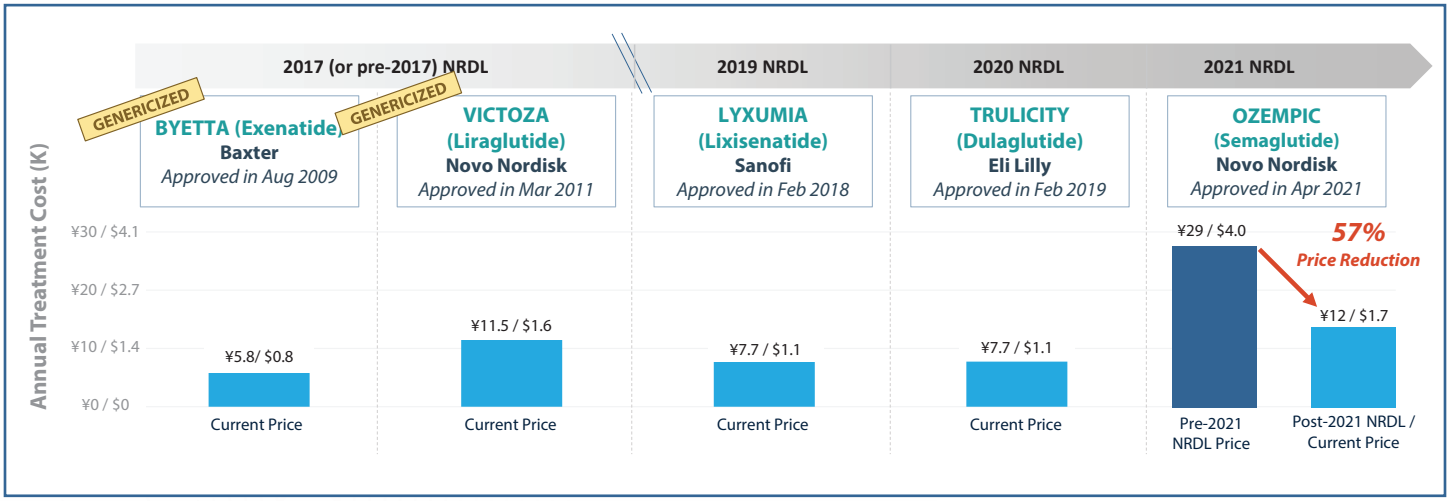


FIGURE 8 | Annual Treatment Costs of NRDL-Listed GLP-1 Receptor Agonists (K, RMB / K, USD)

Key Takeaways

» Overall, we saw a success rate of over 80% in 2021 NRDL negotiations. Out of the 94 products that were listed through price negotiation, 67 were branded drugs being included for the first time. On average, these branded drugs took a 62% price reduction for NRDL inclusion, which is in line with outcomes from past negotiations.

» 40% of the listed products after the 2021 negotiation achieved NRDL inclusion in the same year as approval, signifying an opportunity for early public access after achieving regulatory approval.

» To secure an invitation for negotiation and show willingness to discount, manufacturers may consider pursuing voluntary price reductions just before the NRDL negotiation, an effective tactic that helped several MNC products achieve NRDL listing in 2021.

» The impact of steep price reduction can be balanced with the high patient volume in China as NRDL inclusion removes the affordability barrier for most patients and ensures prioritized access to hospital formulary. For innovative products with significant clinical benefits, the post-NRDL revenue growth trends may continue.

» Currently no other markets officially reference China pricing but MNCs should strategically sequence their global launches as pricing in China may be unofficially considered by certain markets during pricing negotiations.

» Driven by concerns on budget impact and budget sustainability, payers in China have lower willingness to pay for prevalent chronic diseases than for oncology or rare diseases; however, premium pricing can be achieved with robust clinical improvement.

Authors

Rya Zhang | Consultant, Evidence, Value, Access & Pricing

Ms. Zhang has extensive knowledge of emerging markets, especially China. Her experience lies across numerous therapy areas, including oncology and rare diseases. Ms. Zhang has expertise in pricing, market access, payer engagement, evidence generation and launch strategy, and has industry experience at a leading domestic biotech in China.

MS, Health Informatics, Cornell University, U.S.

Flora Chung | Senior Consultant, Evidence, Value, Access & Pricing

Ms. Chung has extensive experience in value, access, and pricing engagements in the EU4+UK and APAC markets, with a particular focus on neurology and immuno-oncology.

MS, International Healthcare Management, Imperial College London, U.K.

Yitong Li, PhD | Senior Consultant, Strategic Advisory

Ms. Li has extensive experience in value & access, and commercial strategy engagement. She has expertise in numerous therapy areas including oncology, chronic infectious diseases, cardiovascular diseases, autoimmune diseases and rare diseases, and deep knowledge about the healthcare system in China, especially pricing and reimbursement.

PhD, Cell Biology & Physiology, University of North Carolina at Chapel Hill, U.S.

Wenting Zhang, PhD | Associate Principal, Evidence, Value, Access & Pricing

Ms. Zhang has over ten years of consulting and industry experience. She has extensive experience across numerous therapy areas including oncology, immunology, neurology, cardiovascular diseases and rare (orphan) diseases.

Ms. Zhang has an in-depth knowledge of the pharmaceutical market in China, particularly in pricing and reimbursement.

PhD, Pharmacology, University of Cambridge, U.K.

Maximilian Hunt | Partner, Evidence, Value, Access & Pricing

Mr. Hunt has extensive experience in pricing, market access, value positioning, and competitive strategy. He advises clients on commercial business issues related to pricing, access, value, and competitive strategy with multiple projects in due diligence, competitive strategic workshops, pricing and contracting and product and portfolio life cycle management.

BS, Biomedical Engineering, Johns Hopkins University, U.S.

About Trinity

Trinity is a trusted strategic commercialization partner, providing evidence-based solutions for the life sciences. With 25 years of experience, Trinity is revolutionizing the commercial model by providing exceptional levels of service, powerful tools and data-driven insights. Trinity's range of products and solutions includes industry-leading benchmarking solutions, powered by TGaS Advisors. To learn more about how Trinity is elevating life sciences and driving evidence to action, visit trinitylifesciences.com.

For more information, please contact us at info@trinitylifesciences.com.