Renal Diseases: Unravelling Complexity To Drive Growth, Peak Sales, and Deals

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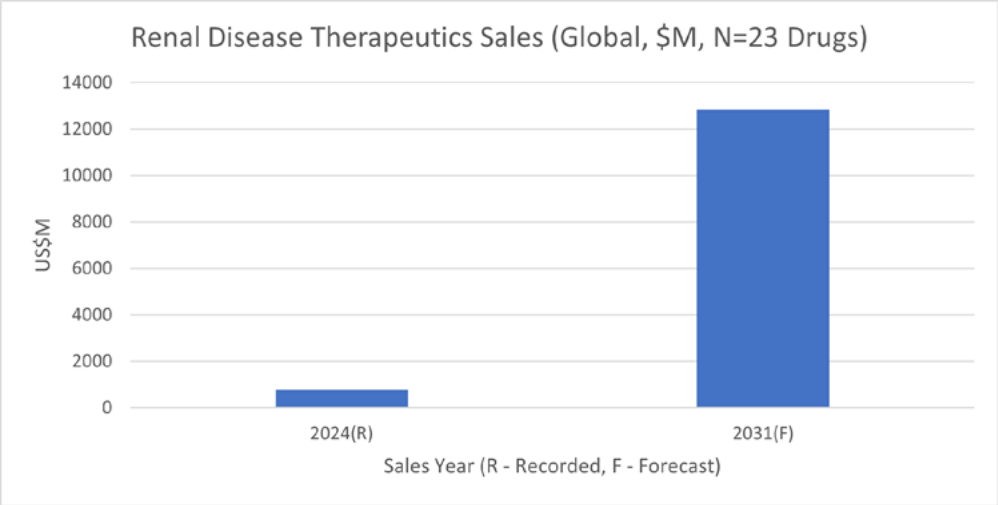
Renal diseases span the spectrum from single gene disorders, which may account for up to 70% of pediatric to 25% of adult ultra-rare and rare disease, to larger allele frequency disorders which often occur as a mixture of idiopathic disease with co-morbidities, defined complex syndromes, and chronic disease secondary to other indications (e.g., hypertension, diabetes etc.). And like all challenging disease there are outliers to the simplified examples listed below (e.g., ultra-rare polygenic C3 glomerulopathy and common allelic variation with large effect size in membranous nephropathy.

Overly Simplified Genetic Spectrum of Renal Diseases

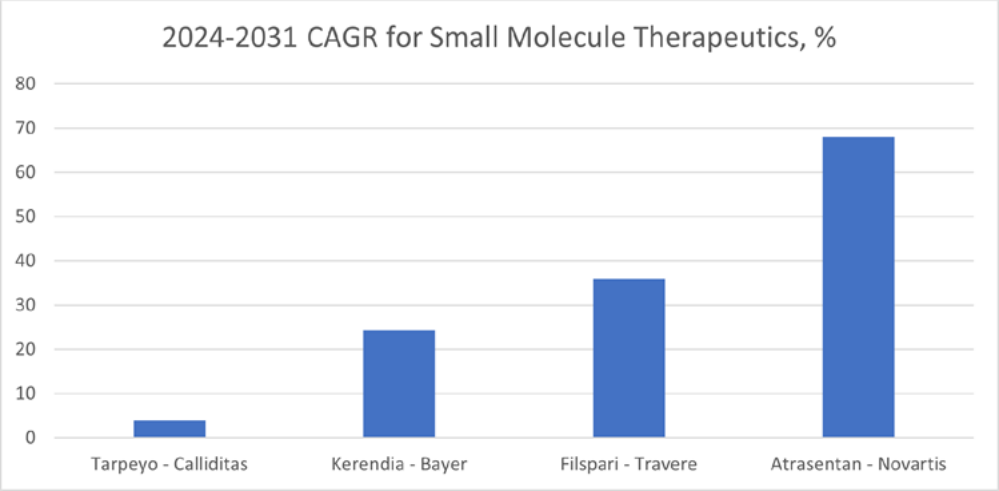
	Ultra-rare	*Rare*	*Moderate*	*Common*
Genetic Effect Size	High	Moderate	Low	Very Low
Allele Frequency	Very Low	Low	Moderate	High
Examples	Alport Syndrome; Fabry Disease	Autosomal Polycystic Kidney Disease (Type 1); Focal Segmental Glomerular Sclerosis [TRPC6]	IgA Nephropathy; Non-Diabetic Kidney Disease	Diabetic Nephropathy; Hypertension

Advances in sequencing, genome-wide associations and polygenic risk scoring algorithms are expected to drive advances in target identification, therapeutic modality diversity and patient selection that will continue to drive growth for curative and chronic treatment approaches.

Regardless of disease etiology, the market for renal diseases (nephropathy) is one of the largest growth areas in the pharmaceutical sector with a global GAGR of **49%** expected for 23 drugs in the 6 to 8 years ending in 2031.



As expected with such a high global CAGR, near average growth for some treatments is bounded by very much lower and much higher growth for others within a given modality type.



Tarpeyo = budesonide DR, a glucocorticoid

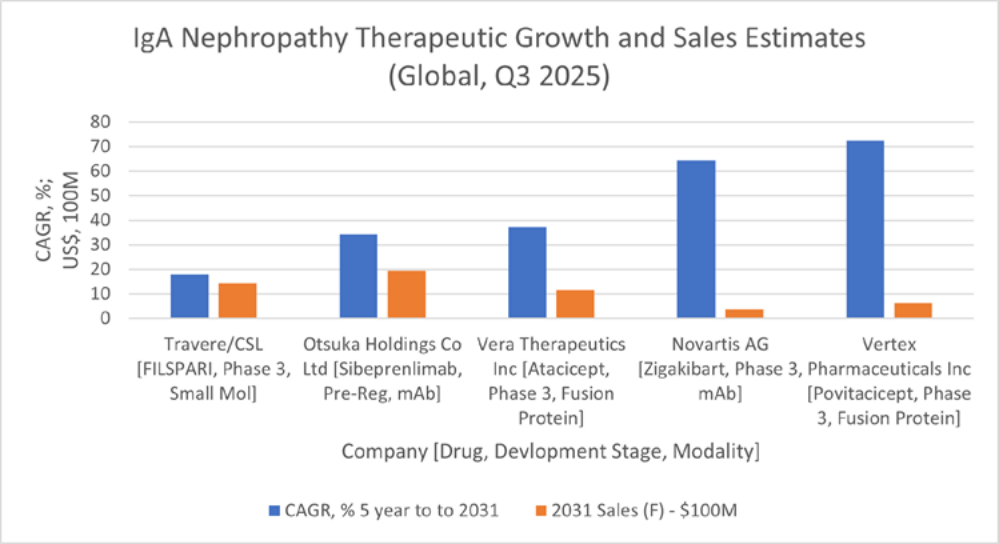
Kerenda = finerenone, a mineralcorticoid

Filspari = sparsetan, antagonist of angiotensin II and endothelin A

Atrasentan =atrasentan, antagonist of endothelin A

This differential perhaps reflects a clinical shift toward layered combination therapy anchored by ACE/ARB and SGLT2 inhibitors, with selective add-ons including endothelin antagonists, APRIL/BAFF inhibitors, complement agents, MRAs, and GLP-1 RA's etc.

Layering tailored to key endpoints such as proteinuria, eGFR slope, as well as patient preferences may hinge on pricing, monitoring burdens, and payer processes to affect sales and sales growth. While this has yet to play out within a clearly defined and highly competitive IgA nephropathy cohort, the data suggests that first market entry (Sibeprelimab vs. Zigkibart; APRIL selective inhibitors) and multiple endpoint durability (Atacicept vs.Povitacicept; BAFF+APRIL dual inhibitors) may be key to higher sales. Target/modality specific impacts on benchmarked endpoints may also drive projected sales (e.g. potential 1st line application of FILSPARI in IgA Nephropathy based on Ibersartan benchmarking; Phase 3 PROJECT).



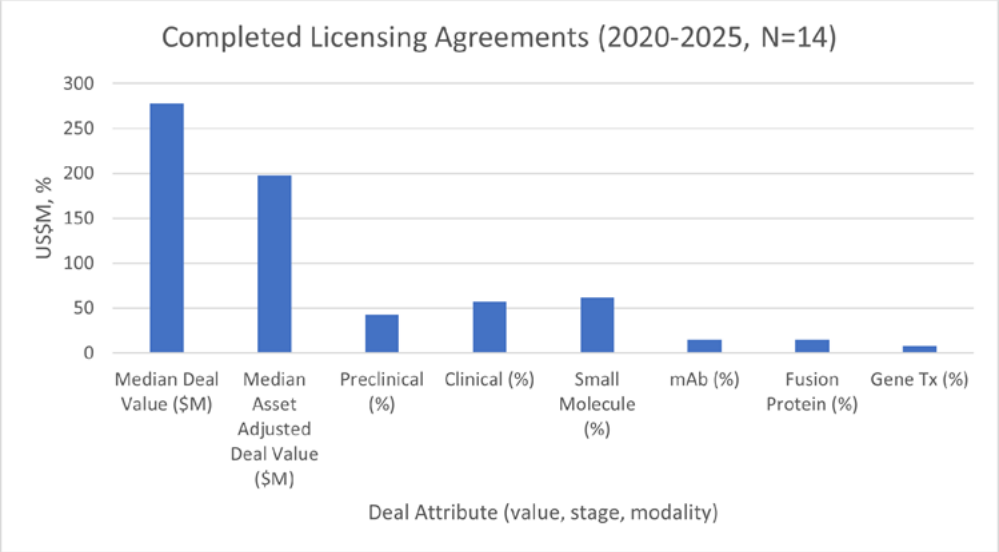
Filspari = sparsetan, antagonist of angiotensin II and endothelin A

Sibeprenlimab = APRIL antibody

Atrasentan =atrasentan, antagonist of endothelin A

Zigakibart = APRIL antibody

Povetacicept = BAFF APRIL inhibitor

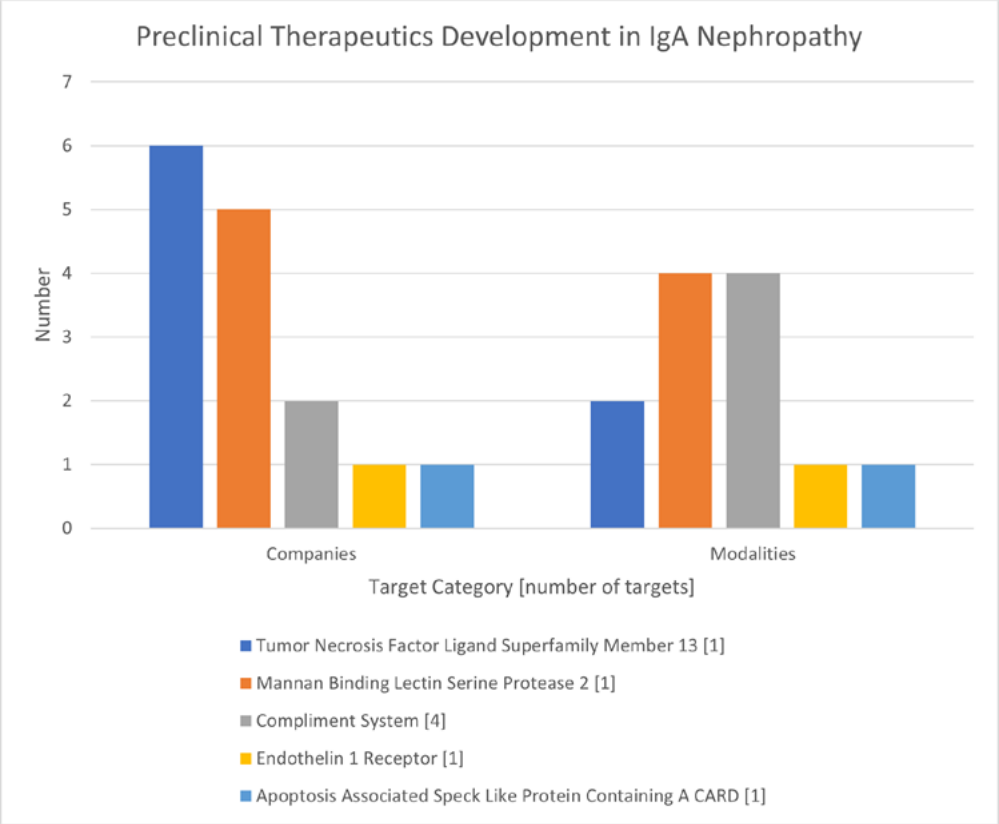


Partnerships and asset transactions in renal disease were less well defined in the 2020 to 2025 period but were marked by several large co-development collaboration partnerships with asset normalized total deal values of US$175M (Flagship Pioneering and Pfizer) and US$1B (Eli Lilly and Evotec) for discovery stage assets.

Acquisitions in the renal disease space underscore the high value ascribed to late-stage clinical programs, particularly where global rights are retained. Complement inhibitors are expected to continue to draw attention with marketed (Apellis, C3 -pegcetacoplan ; Alexion, C5 – ravulizumab and Factor D -danicopan) and clinical stage products (Shanghai Argo Pharmaceutical Co. Ltd., Factor B inhibitor -antisense).

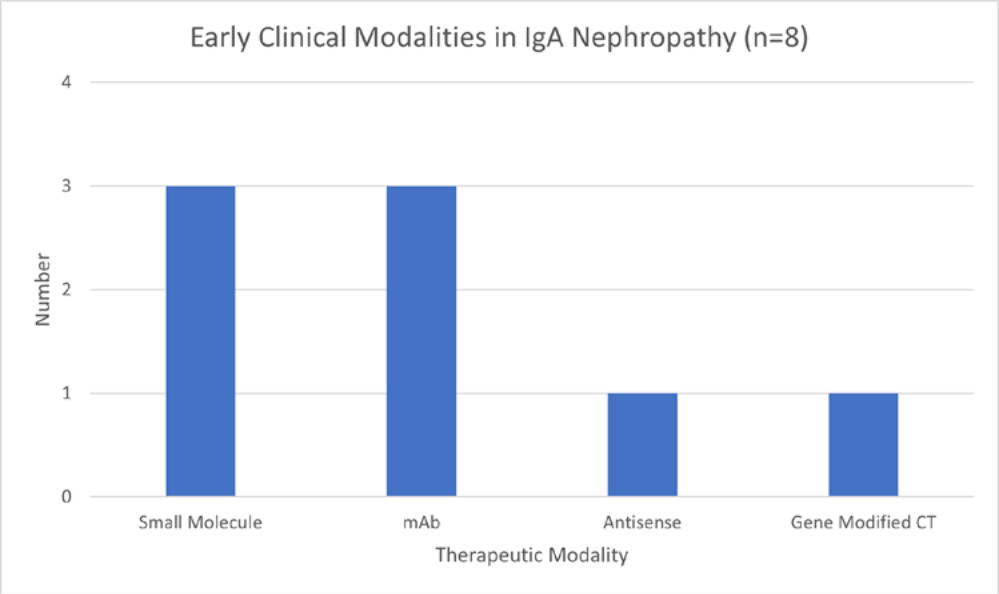
Acquirer–Target	Asset(s) / Rationale in Renal Disease	Consideration
Vertex–Alpine Immune Sciences (Nov 2025)	Acquisition of **povetacicept** platform spanning IgAN/pMN	**$5.0bn** cash purchase price
Chugai–Renalys Pharma (Oct 2025)	Secures exclusive rights to commercialize **sparsentan** in Japan, South Korea and Taiwan	**~US$98 M** closing cash + up to **~US$102M** earn-outs and sales-linked consideration
Amgen–ChemoCentryx (Aug 2022)	Adds **TAVNEOS/avacopan** (C5aR) marketed in ANCA-associated vasculitis	**$3.7bn**

If we circle back to the highly competitive clinical/market space in IgA Nephropathy and look at the most advanced active preclinical development programs for that indication we see a spread across mAb (9), Fusion Protein (5), Antisense Oligonucleotide (4) and Protein (1).



As mentioned in the previous section the complement system is of growing interest and this is underscored in the preclinical space by a company like Shanghai Alebund Pharmaceuticals that is pursuing multiple modalities across the four complement system targets identified (C3, C5, Factor B, Immunoglobulin A).

Of eight companies with defined early clinical programs (Phase 1 and 2) in IgA nephropathy, there are eight different targets spread across 4 modalities. Endothelin-1 receptor antagonists cut across preclinical, early clinical, and late clinical/marketed stages of development.



Key Takeaways

Target identification, diagnosis, therapeutic development, and patient selection strategies will accelerate on the back of advancements in **multi-omic integration, risk algorithm creation and modality targeting** to drive growth in the renal diseases space.

IgA nephropathy emerges as a very competitive disease battleground with at least four therapies (FILSPARI, Fabhalta, Vanrafia, Tarpeyo) utilizing distinct mechanisms from dual receptor blockade to complement inhibition, while late-stage pipeline candidates like povetacicept and atacicept target BAFF/APRIL pathways with potential for best-in-class differentiation.

Ultra-rare complement-mediated diseases gain first targeted therapies as EMPAVELI becomes the first approved C3 inhibitor for C3 glomerulopathy and IC-MPGN, establishing a new treatment paradigm for previously untreatable conditions with significant unmet medical

need. Inhibitors of additional compliment targets are advancing preclinically and in early clinical development.

SGLT2 inhibitors achieve unprecedented guideline endorsement with KDIGO 2024 CKD guidelines recommending class 1a use irrespective of diabetes status, fundamentally reshaping first-line CKD treatment and expanding addressable patient populations beyond traditional diabetic indications.

Licensing deals reflect massive upfront commitments for novel targets with Arbor-Chiesi's CRISPR gene editing deal reaching $115M upfront and $2B in milestones, while Vertex's $5.0B acquisition of Alpine's povetacicept platform demonstrates strategic consolidation around breakthrough mechanisms. Global rights will drive higher overall deal value and royalty ceilings.

Clinical practice shifts toward layered combination strategies as nephrologists describe anchoring therapy with ACE/ARB and SGLT2 inhibitors, then adding selective agents based on proteinuria, eGFR slope, and patient preferences.

To stay up to date I highly recommend following the KDIGO guidelines at Kidney International