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Zacks Small-Cap Research
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Durect Corp (DRRX-NASDAQ)

Favorable FDA Decision on POSIMIR Would Likely Mean Significant Upside to Our Model

We value DRRX using sum-of-the-parts, with most of the value related to DUR-928 based on pricing of recent NASH-targeted M&A transactions as a proxy. Our methodology also includes DCF of DRRX's current cash-generating products and earn-outs.

Current Price (06/27/19)	$0.68
Valuation	**$5.50**

OUTLOOK

Durect announced that they submitted a full response to FDA's Complete Response Letter for POSIMIR. The decision to submit a response to the CRL was based on Dr. Simon's (a physician and previous Director of FDA's Analgesic, Anti-inflammatory and Ophthalmologic Drug Products division) review of the PERSIST data – which presumably means that he believes the package that they compiled and submitted was sufficient (based on his insight and experience with FDA's Analgesic division, particularly in terms of what they need as support) to warrant eventual approval of the POSIMIR NDA. As we had removed POSIMIR from our model, a favorable response from FDA would likely provide upside to our estimates. The market for POSIMIR could be substantial and, as such, potential revisions to our model could be as well. As such, we will be eagerly awaiting word from FDA. Similar to POSIMIR, bupivacaine is the active ingredient in Pacira Biosciences' Exparel, which is also indicated for postsurgical pain relief. Exparel (bupivacaine liposome injectable suspension) generated $331M in sales in 2018 which analysts forecast will grow at a CAGR of almost 11% to $615M by the year 2024. Exparel accounts for 100% of the revenue of Pacira Biosciences', which currently trades at a market capitalization of $1.8 billion.

SUMMARY DATA

52-Week High	**$1.75**
52-Week Low	**$0.46**
One-Year Return (%)	**-60.00**
Beta	**1.89**
Average Daily Volume (sh)	**662,748**
Shares Outstanding (mil)	**192**
Market Capitalization ($mil)	**$130**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**44**
Insider Ownership (%)	**10**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**14.3**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2019 Estimate	**N/A**
P/E using 2020 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	4.6 A	4.3 A	20.8 A	19.5 A	49.2 A
2018	3.5 A	3.4 A	8.0 A	3.6 A	18.6 A
2019	4.1 A	4.2 E	3.5 E	4.2 E	16.1 E
2020					18.1 E

Price/Sales Ratio (Industry = 2.5x)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	-$0.06 A	-$0.07 A	$0.04 A	$0.05 A	-$0.03 A
2018	-$0.05 A	-$0.04 A	-$0.02 A	-$0.05 A	-$0.16 A
2019	-$0.04 A	-$0.05 E	-$0.05 E	-$0.05 E	-$0.19 E
2020					-$0.21 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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WHAT'S NEW

POSIMIR CRL Response Made. Favorable Decision Would Likely Mean Significant Upside to Our Model
This morning Durect announced that they submitted a full response to FDA's Complete Response Letter for POSIMIR, which Durect received in February 2014. POSIMIR is the company's investigational post-operative pain relief depot that utilizes the company's patented SABER technology and is intended to deliver bupivacaine to provide three days of pain relief after surgery.

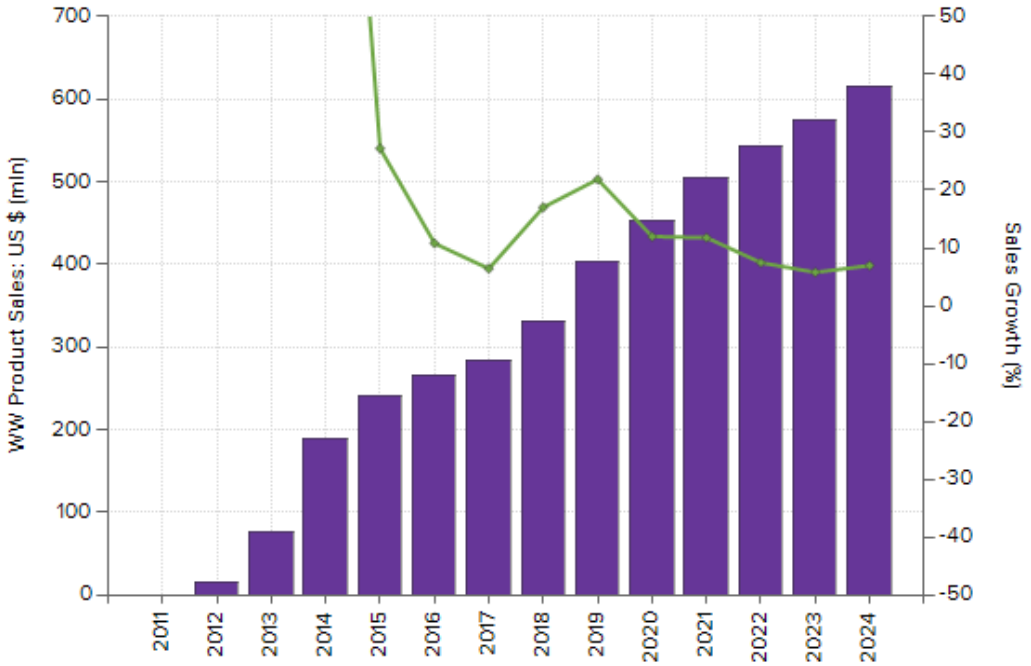
As a reminder DRRX submitted an NDA ((via 505(b)(2) pathway)) to FDA for POSIMIR in April 2013. FDA responded in February 2014 with a Complete Response Letter. Following interaction with the agency, Durect conducted and completed a Phase 3 clinical trial of POSIMIR (PERSIST trial). As reported in October 2017, while results favored POSIMIR, the trial failed to meet its primary endpoint of a statistically significant reduction in pain on movement over the first 48 hours after surgery as compared to standard bupivacaine HCI. To-date Durect has completed a total of 16 clinical studies with POSIMIR.

DRRX recently engaged Dr. Lee S. Simon, a physician and previous (2001 – 2003) Director of FDA's Analgesic, Anti-inflammatory and Ophthalmologic Drug Products division, to evaluate potential next-steps with POSIMIR. The decision to submit a response to the CRL was based on Dr. Simon's review of the PERSIST data – which presumably means that he believes the package that they compiled and submitted was sufficient (based on his insight and experience with FDA's Analgesic division, particularly in terms of what they need as support) to warrant eventual approval of the POSIMIR NDA. Per Dr. Simon's comment in this morning's press release, "We believe that the submitted response to the CRL includes multiple positive adequate and well controlled trials and addresses the issues raised in the FDA's Complete Response Letter."

Importantly, it is our understanding that approval largely hinges on demonstration of sufficient safety and that failure to meet the efficacy endpoint in PERSIST may not be particularly relevant. Further, DRRX's CRL response includes substantive additional data that supports safety of the drug. FDA's response is anticipated within six months – which means we may not hear back until sometime near year-end.

As we had removed POSIMIR from our model, a favorable response from FDA would likely provide upside to our estimates. The market for POSIMIR could be substantial and, as such, potential revisions to our model could be as well. As such, we will be eagerly awaiting word from FDA.

Historical and Consensus Analysts' Estimated Sales of Exparel



Source: EvaluatePharma

Similar to POSIMIR, bupivacaine is the active ingredient in Pacira Biosciences' Exparel, which is also indicated for postsurgical pain relief. Exparel (bupivacaine liposome injectable suspension) generated $331M in sales in 2018 (effectively all of which was from the U.S.) which analysts forecast will grow at a CAGR of almost 11% to $615M by the year 2024. Exparel accounts for 100% of the revenue of Pacira Biosciences' (NASDAQ: PCRX), which currently trades at a market capitalization of $1.8 billion.

90mg Cohort Completes, DEC OKs 150mg Dosing of Severe AH Patients in Phase 2a Study with IV DUR-928
DUR-928, which we think could have platform-like utility, is where we continue to believe most of the upside value lies in DRRX. DUR-928 is being investigated in several formulations and potential applications including oral, intravenous and topical formulas and in indications such NASH, alcoholic hepatitis (AH) and psoriasis.

On June 18th DRRX announced that the 90mg cohort with severe alcoholic hepatitis patients completed dosing and the Dose Escalation Committee approved enrollment of the 150mg severe AH cohort in their ongoing AH Phase 2a study with IV DUR-928. Importantly, not only do results appear to continue to be as hoped, but DRRX continues to hit their anticipated timelines with this study.

DRRX's press release notes that the preliminary data from the 90mg severe AH patients are consistent with the 30mg (eight patients: four moderate AH, four severe AH) and 90mg (two patients: one moderate, one severe) patients that they reported on in May. As a reminder, management characterized those results (which we have included as a refresher below) as "…highly compelling, indicating a potentially potent efficacy signal and lack of toxicity."

As we noted in our Q1 update in May, if the full study data further supports the safety and effectiveness of DUR-928 and largely confirms the findings from the initial nine patients, we think that could represent a value inflection event for the share price. As such, we think this recent announcement is of real significance.

Refresher on results of AH Phase 2a Study with IV DUR-928 announced in May (note this does not include the 90mg severe AH group which just completed)…

AH Phase 2a study with IV DUR-928

- Includes two patient cohorts;
  - Part A: moderate AH at three dose levels; 30mg, 90mg and 150mg (n=4 per dose cohort) and
  - Part B: severe AH at 30mg, 90mg and possibly a 150mg dose (n=4 per dose cohort)
- Preliminary data on first 10 patients (8 30mg: 4 moderate, 4 severe and 2 90mg: 1 moderate, 1 severe) was reported on May 7th. ***Results in our opinion are highly compelling, indicating a potentially potent efficacy signal and lack of toxicity.*** Our enthusiasm is further bolstered by supportive comments from AH KOLs (which joined the call)
- Results were compared to ongoing Univ of Louisville (UL) study (led by Dr McClain) as a proxy comparator arm. UL study patients' (n=15) therapy consisted of either supportive care or supportive care with corticosteroids
- Baseline average MELD scores (i.e. AH severity) were similar among 10 DUR-928 patients and 15 UL patients
- ***Results showed*** (data was available for 9 of initial 10 DUR-928 patients). Along with safety, which showed no issues through the first 10 patients, results included;
  - Lille scores: used in clinical practice to assess AH prognosis after 7 days of treatment. Studies have shown Lille score below 0.45 is associated with 85% 6-month survival rate and above 0.45 is associated with 25% 6-month survival rate
    - DUR-928 (n=9): median Lille score of 0.04 (range 0.01-0.19) at Day 7
    - UL (n=15): median Lille score of 0.41 (range 0.02-0.96) at Day 7
    - The differences (i.e. DUR-928 lower Lille scores vs UL) were statistically significant (p=0.002, Wilcoxon's Rank Sum)
  - Bilirubin levels: bilirubin is a determinant for liver functioning (lower is better) and is used in practice as a marker for clinical outcomes of AH patients
    - DUR-928: median bilirubin fell from baseline by 16% at Day 7 (n=9) and by 41% at Day 28 (n=8)
    - UL (n=15) median bilirubin fell from bassline by 3% at Day 7 and by 35% at Day 28

    - The change from baseline with DUR-928 was statistically significant (p=0.04) at both days (and was not statistically different with UL at either day)
- Model of End-Stage Liver Disease (MELD) scores: used in clinical practice as an assessment of severity of AH and patient prognosis
    - DUR-928: median MELD fell from baseline by 4% at Day 7 (n=9) and fell by 21% at Day 28 (n=8)
    - UL (n=15): median MELD increased from baseline by 4% at Day 7 and fell by 6% at Day 28
    - The change from baseline differences with DUR-928 was statistically significant at Day 28 (p=0.03) and trended towards significant reduction by Day 7
- Among the comments from the KOLs on the call that lend support for these results as well as the potential market for DUR-928 in AH include;
    - Regarding unmet need for effective AH therapy (for context, given the lack of better alternatives, corticosteroids are currently used as a first-line therapy for AH)[1]
        - "There really are no therapies for this [i.e. AH]. Corticosteroids, I'm not convinced they work at all actually."
        - "There was a recent randomized controlled trial that really did not show statistically significant benefit with [corticosteroids] product. And it's been out for 40 years, and we rarely use it at all at Northwestern."
        - "And liver transplant, which is the other way you can save people who are on liver failure, these patients are in general contraindicated from liver transplant."
    - Regarding these preliminary results (relative to safety and efficacy)[2]
        - [These results are from] "[s]mall number of patients but give us tremendous hope in this study drug."
        - "And the beautiful thing about it so far is the safety. We went from the 30-milligram dose to the 90, and we have -- we haven't seen any significant signals of any safety issues."
        - "And so far, every patient we've put in my group that had a response to the treatment. And the main response we see bilirubin improving. Once bilirubin is improving, everything starts to change. The MELD score changes. The MELD rate changes. Whatever scoring system you use, bilirubin is a key element in this disease, and we have been seeing improvement in the bilirubin within the first few days."
        - "Actually, this is my first time to see the collected data together. So I'm very enthusiastic."

Next steps

- Hope to complete the trial this year
    - DRRX noted on the Q1 call (in May) that if the data from the remaining patients is positive that they will plan to present the data at AASLD in November
    - We also note that if the full study data further supports the safety and effectiveness of DUR-928 and largely confirms the findings from these initial patients, we think that could represent a value inflection event for the share price
- If all goes well, following completion of the study, DRRX will meet with FDA regarding pivotal trial design and commence the pivotal program in 2020
- The severity of AH, high mortality rate and lack of effective therapies for the disease could bold well for FDA fast-track designation of a pivotal program

Valuation

DRRX sold 29M shares at $0.52/share for net proceeds of ~$15M. The transaction closed on or about June 24th. While we had anticipated a raise, we had modeled it at slightly higher pricing and for the bulk of the shares to be sold in 2020. The increase in near-term share count relative to our projections has the effect of moving our calculated target price from $6.00 to $5.50/share. But we continue to think the shares trade at a significant discount to fair value.

[1] Professor of Medicine and Surgery with the Division of Hepatology at Northwestern University, a Feinberg School Of Medicine. He also serves as the Chief of Transplant Hepatology. Dr. Flamm has published and speaks widely in the field of hepatic diseases.

[2] Dr Tarek Hassanein. Professor of Medicine at University of California San Diego School of Medicine. Dr. Hassanein was instrumental in establishing three major liver transplant programs. http://www.livercenters.com/about-sclc/meet-our-staff/

PROJECTED INCOME STATEMENT

Durect Corporation

DURECT Corp	Q1	Q2	Q3	Q4	2018 A	Q1	Q2	Q3	Q4	2019 E	2020 E	2021 E
PERSERIS Earn-outs (US)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.1	$0.2	$0.2	$0.5	$2.2	$3.6
YOY Growth	-	-	-	-	-	-	-	-	-	-	333.9%	63.6%
PERSERIS (Ex-US)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	
ORADUR-ADHD (DRRX rights)	$0	$0	$0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	
ORADUR-ADHD (Orient Pharma) Rylty	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.1	$0.1	$0.2	$0.4	$0.7
YOY Growth	-	-	-	-	-	-	-	-	-	-	135.3%	75.0%
DUR-928	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-
Alzet Pumps & Lactel Polymers	$2.4	$2.8	$2.3	$2.9	$10.4	$2.6	$2.9	$2.6	$3.2	$11.2	$12.5	$13.0
YOY Growth	-42.1%	-9.3%	-11.3%	-12.6%	-20.9%	10.0%	3.0%	8.7%	10.4%	8.0%	11.8%	4.0%
Total Product Sales	$2.4	$2.8	$2.3	$2.9	$10.4	$2.6	$2.9	$2.6	$3.2	$11.2	$12.5	$13.0
YOY Growth	-42.1%	-9.3%	-11.3%	-12.6%	-20.9%	10.0%	3.0%	8.7%	10.4%	8.0%	11.8%	4.0%
Collaborative Revenue	$1.1	$0.6	$5.7	$0.8	$8.2	$1.5	$1.3	$1.0	$1.1	$4.9	$5.6	$10.0
YOY Growth	152.5%	-49.1%	1.6%	-95.2%	-65.2%	36.9%	107.8%	-83.1%	38.1%	-40.7%	15.0%	78.6%
Revenue from sale of IP rights	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	$3.5	$3.4	$8.0	$3.6	$18.6	$4.1	$4.2	$3.5	$4.2	$16.1	$18.1	$23.0
YOY Growth	-23.6%	-21.0%	-61.3%	-81.4%	-62.2%	18.4%	22.8%	-56.3%	16.3%	-13.5%	12.8%	27.1%
Cost of Goods Sold	$1.2	$1.1	$0.9	$1.1	$4.3	$1.1	$1.1	$0.9	$1.2	$4.4	$4.5	$4.6
Product Gross Margin	50.9%	60.8%	61.1%	61.7%	58.8%	51.2%	62.1%	63.6%	61.4%	65.0%	64.1%	65.0%
SG&A	$3.2	$2.8	$2.9	$3.5	$12.4	$3.5	$3.2	$3.3	$3.6	$13.6	$16.1	$18.7
% SG&A	91.6%	82.5%	35.7%	97.6%	66.9%	83.6%	76.4%	94.0%	85.3%	84.4%	89.0%	81.3%
R&D	$7.0	$6.1	$6.5	$5.9	$25.5	$6.3	$7.4	$7.7	$8.0	$29.4	$36.4	$38.1
% R&D	199.3%	179.3%	81.4%	162.3%	137.4%	151.3%	176.6%	219.4%	189.6%	182.9%	201.1%	165.7%
Operating Income	($7.8)	($6.6)	($2.3)	($6.9)	($23.6)	($6.7)	($7.5)	($8.4)	($8.6)	($31.2)	($38.9)	($38.4)
Operating Margin	-	-	-	-	-	-	-	-	-	-	-	-
Interest & Other Net	($0.5)	($0.4)	($0.4)	($0.4)	($1.7)	($0.4)	($0.5)	($0.6)	($0.6)	($2.1)	($2.4)	($1.7)
Pre-Tax Income	($8.3)	($7.0)	($2.7)	($7.3)	($25.3)	($7.1)	($8.0)	($9.0)	($9.2)	($33.3)	($41.3)	($40.1)
Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Net Income	($8.3)	($7.0)	($2.7)	($7.3)	($25.3)	($7.1)	($8.0)	($9.0)	($9.2)	($33.3)	($41.3)	($40.1)
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-
Reported EPS	($0.05)	($0.04)	($0.02)	($0.05)	($0.16)	($0.04)	($0.05)	($0.05)	($0.05)	($0.19)	($0.21)	($0.20)
YOY Growth					-	-	-	-	-	-	-	
Shares Outstanding	153.6	161.6	162.0	162.0	159.8	162.1	164.0	189.4	190.0	176.4	196.0	205.0

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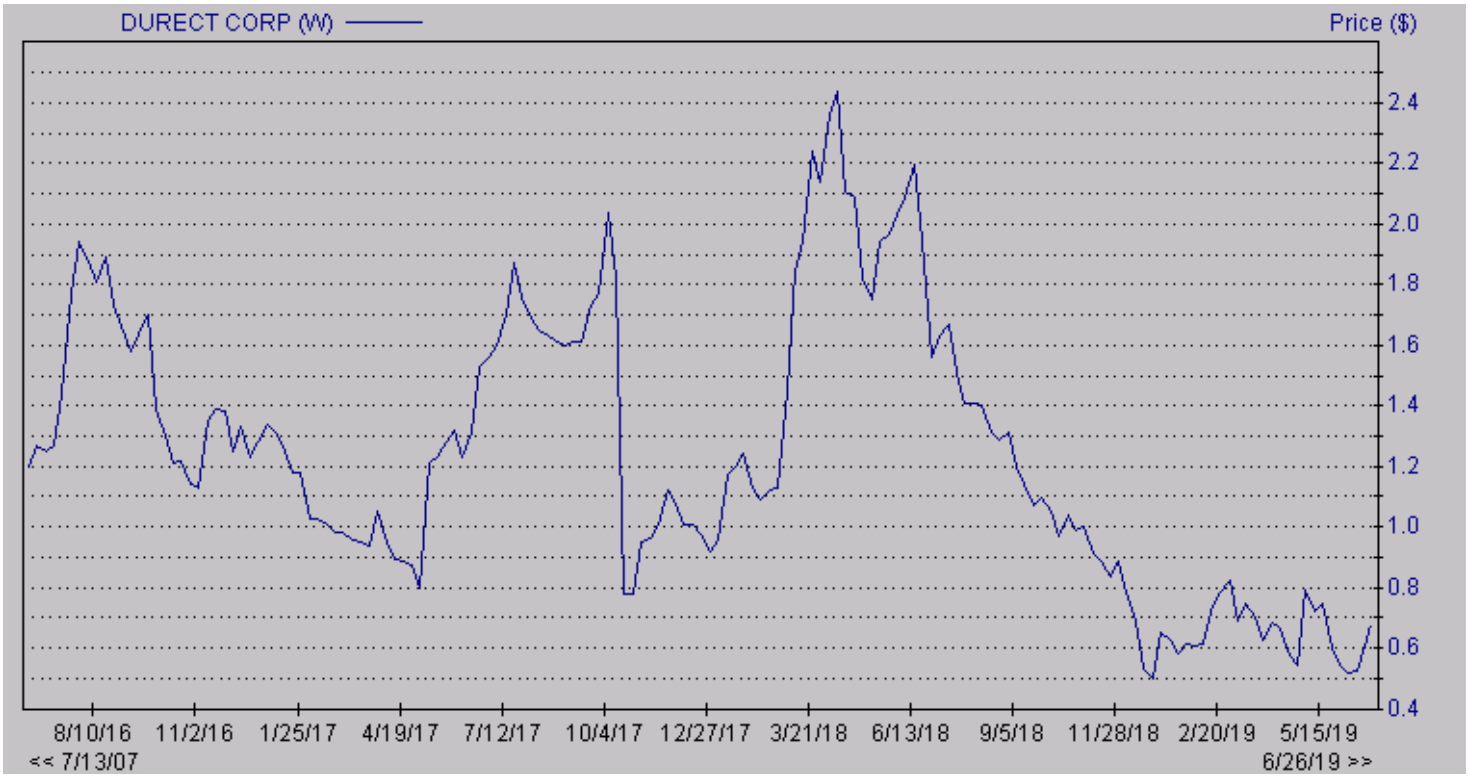

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